Factors affecting patients' decision-making and the development of a prognostic model in total knee replacement surgery

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Table of Contents

List of Tables

List of Figures

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Declarations

This thesis is submitted to the University of Warwick in support of my application for the degree of Doctor of Philosophy. It has been compiled solely by me and has not been submitted in any previous application for any degree.

The work presented (including data generated and data analysis) was carried out by me except in the cases outlined below:

- Chapter 2: Dr A. Realpe provided independent data extraction. Dr D. Barlow provided independent assessment of references for inclusion.
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Research training

I have undertaken the following research training during my period of study:

Internal course	Date
Statistics and Epidemiology (before registration for PhD)	12-16th November 2012
Design, Analysis and Interpretation of Epidemiological Research	9-13th February 2014
NVivo 10 -- an overview	7th October 2014
SPSS -- an overview	9th October 2014
SPSS -- Elementary Statistical Methods	16th October 2014
Microsoft Access -- Using databases	7th November 2014
SPSS -- Data operations	14th November 2014
Chief Investigator Course	15th January 2015

External courses, awards and scholarships	Date
Qualitative Research Design, NatCen Learning, London.	30-31st October 2012
Postgraduate Diploma in Medical Education. The Association of Business Practitioners/The Royal College of Physicians and Surgeons of Glasgow.	Awarded 17th of January 2013
Individual and Group Interviews (Advanced Training Course). Nottingham University Doctoral Training Centre.	11-12th February 2013
National Institute for Health and Care Excellence (NICE) Scholarship	May 2013 – May 2014
ANOVA, Centre for applied statistics, UCL.	8th December 2014
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Logistic Regression, Centre for applied statistics, UCL.	9th February 2015
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Annual Clinical Academic Training Research Meeting	30th January 2013
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Abstract

Osteoarthritis of the knee is a common condition, affecting more than 10% of the population aged over 55 years. It can lead to pain, functional loss, and a reduction in the quality of life. Total knee replacement is a common procedure for those with severe osteoarthritis with over 90,000 procedures performed each year in the UK; however, around 20% of patients are dissatisfied with the outcome. How to identify these patients pre-operatively is a research priority, as set out by the British Orthopaedic Association, Arthritis Research U.K., and the National Institute for Health and Care Excellence. The effect such an advance would have on patients' decision-making is not known.

Therefore, in this thesis I set out to understand the factors important to patients when contemplating a knee replacement, how an outcome prediction tool could affect that process, and then go on to develop an prognostic model for use in patients considering a total knee replacement.

I first performed a systematic review of factors that influence patient's decision-making; I then describe two qualitative projects, the first developed a model of decision-making, the second investigated how providing predictions of outcome could affect expectations and decision-making.

This information, combined with a systematic review of the factors that affect outcome in knee replacements, allowed me to develop a multicentre cohort study designed to generate a prognostic model. This study recruited 600 patients, and the linear regression model accounts for 36% of the variability in outcome – more than any previous study.

This thesis provides a better understanding of patients' decision-making, which should facilitate doctor-patient communication. I describe a model that can predict more variability in outcome than any previous models. The usefulness of the model in individual prediction and potential future areas of study include how more variability could be incorporated, how to develop such a model into a prediction tool, and other approaches to addressing poor outcomes after total knee replacement.

Abbreviations

ACI	Autologous Chondrocyte Implantation
ACL	Anterior Cruciate Ligament
ACL	Anterior Cruciate Ligament
AIC	Akaike Information Criteria
ANOVA	Analysis of Variance
anti-CCP	anti-Cyclic Citrullinated Peptide
ARC	American College of Rheumatology
BASK	British Association for Surgery of the Knee
BMI	Body Mass Index
BOA	British Orthopaedic Association
BPT	Best Practice Tariff
CBT	Cognitive Behavioural Therapy
CP	Citrullinated Protein
DNA	Did Not Attend
DoH	Department of Health
EQ 5D	EuroQol 5 Dimensions
GEH	George Elliot Hospital
HADS	Hospital Anxiety and Depression Score
HES	Hospital Episode Statistics
IMD	Index of Multiple Deprivation
ISRCTN	International Standard Randomised Controlled Trial Number
KOOS	Knee injury and Osteoarthritis Outcome Score
KOPS	Knee Outcome Prediction Study
KOS/ADLS	Knee Outcome Survey Activities of Daily Living Scale
KSRS	Knee Society Rating System
KSS	Knee Society Score
MACI	Matrix-induced Autologous Chondrocyte Implantation
MAR	Missing At Random
MCAR	Missing Completely at Random
MCID	Minimal Clinically Important Difference
MCS	Mental Component Score
MF	Mental Functioning
MNAR	Missing Not At Random
MRI	Magnetic Resonance Imaging
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
NJR	National Joint Registry
NOS	Newcastle Ottawa Scale
OA	Osteoarthritis
OKS	Oxford Knee Score
OKS	Oxford Knee Score
PCS	Pysical Component Score

PCT	Primary Care Trust
PDAs	Patient Decision Aids
PF	Physical Functioning
PROMs	Patient Reported Outcome Measures
QALY	Quality Adjusted Life year
QIPP	Quality, Innovation, Productivity, and Prevention
RCT	Randomised Controlled Trial
RCT	Randomised Controlled Trial
sd	Standard Deviation
SE	Standard Error
SF-12	Short Form 12
SF-36	Short Form 36
UHCW	University Hospitals of Coventry and Warwickshire
UNTRAP	University/User Teaching and Research Action Partnership
WOMAC	Western Ontario and McMaster Universities Arthritis Index

Chapter 1: Introduction and background

This chapter discusses the epidemiology of knee osteoarthritis and the treatment of it, focusing on the current issues facing the provision of knee replacement surgery, namely: variability in outcome, increasing demands with financial constrains, and variability in utilisation.

1.1 Declarations

Aspects of this chapter have been published:

T. Barlow, T. Clarke, M. Dunbar, A Metcalfe, D. Griffin. The effect of expectation on satisfaction in total knee replacements: a systematic review. SpringerPlus 2016 **5**:167. DOI: 10.1186/s40064-016-1804-6

Aspects of this chapter have been presented as a poster at a regional meeting:

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1.2 Osteoarthritis of the knee

1.2.1 Definition

Osteoarthritis (OA) literally means inflammation of the bone and joint. It has been defined in many different ways, including:

- "The majority of peripheral joint pain in older adults (especially at the knee, hip, hand and foot), once the rarer types of arthritis where inflammation is predominant (e.g. rheumatoid arthritis and psoriatic arthritis) are excluded."[1]

- "A clinical syndrome of joint pain accompanied by varying degrees of functional limitation and reduced quality of life"[2]

Additionally, OA has been defined by the morphological changes that it produces. Plain radiograph findings include joint space narrowing, osteophytes, subchondral sclerosis, and bone cysts.[3] Figure 1 demonstrates some of these common radiographic findings. In addition to plain radiography, Magnetic Resonance Imaging (MRI) criteria now exist.[1,3]

Figure 1: Plain radiograph of an osteoarthritic knee demonstrating osteophytes, reduced joint space, and sclerosis. Subchondral cysts are not present. Reproduced with permission from http://www.lookfordiagnosis.com.

1.2.2 Diagnosis

As to be expected from the variation in definitions of OA, there are varying criteria for diagnosing knee OA.[3] These range from using radiographic criteria alone (although there is no reliable correlation between radiographic presence and/or severity of symptoms),[3] clinical symptoms alone (as recommended by NICE),[2] or a combination approach (as described by the American College of Rheumatology; ARC).[4] The ARC also includes laboratory finding (predominantly excluding other causes of arthritis; e.g. Erythrocyte Sedimentation Rate less than 40mm/hour).[5] Recently, there has been a large amount of effort in identifying biomarkers specific for early OA. Recent success has been met by measuring plasma/serum citrullinated protein (CP), anti-cyclic citrullinated peptide (anti-CCP) antibody and hydroxyproline. The authors report not only a sensitive test for early arthritis, but also one that is specific in distinguishing early OA from Rheumatoid arthritis. However, further validation is needed.[6]

1.2.3 Classification

Classification of knee OA can be based on site (medial, lateral, or patellofemoral), radiological features, or aetiology.[3,5] In relation to aetiology, OA has traditionally been divided into primary (idiopathic) and secondary. Secondary OA can be further sub-divided into post-traumatic, congenital or developmental diseases, calcium deposition disease, other bone and joint disorders, and other diseases.[5] However, as discussed in the next section, the traditional division of OA into primary and secondary is now being challenged as our understanding of the pathophysiology and risk factors for the development and progression of knee OA improves.[7]

1.2.4 Risk factors and pathogenesis

Risk factors for the development of knee OA have been widely studied and a meta-analysis conducted in 2015 demonstrated that increased Body Mass Index (BMI), previous knee injury, presence of Heberden's nodes/hand OA, female gender, older age, intensive physical activity, certain physical occupational activities (e.g. kneeling), and increased bone mineral density all predispose to OA knee.[8] Additionally, the authors concluded that good mental health, oestrogen, sitting for more than two hours a day, smoking, and having an index finger longer than the ring finger may reduce the risk of OA, but the evidence for these factors is weaker.[8] Factors not included in this meta-analysis include biomechanical factors and genetic factors. There appears to be a genetic predisposition to OA development, with studies suggesting multiple genes acting in concert.[1]

Malalignment has been demonstrated to increase the risk of OA, as has ligament and meniscal injury and articular fracture.[3] It may be that these factors are not truly primary OA – this has led to some authors suggesting that OA is in fact one disease process with a complex interplay between genetic, environmental, and psychological processes, or represents several conditions with a common pathological endpoint.[7] Inconsistency regarding factors that predispose to developing OA compared with factors that cause the progression of the disease supports this view. For example, osteoporosis may be protective against developing OA knee, but may lead to faster progression.[8,9]

With disagreement over the classification of OA, much work has been carried out trying to understand the pathophysiology. Cartilage changes include increased synthesis of matrix components by chondrocytes along with proteolytic degradation of those components (i.e. increased turn over). Changes in the bone are not as well understood, and the interplay between cartilage and bone changes is likewise poorly understood. What is clear is that inflammatory mediators play a role in OA, and a systemic element is likely. This could be a target for future treatments.[7] Therefore, there is a general consensus that the "wear and tear" model of OA is now outdated.[1,3] Instead, there is an interaction between risk factors; microtrauma of the knee leads to an inflammatory response and subsequently a repair process – the so called "tear, flare, repair".[1] Therefore the disease is one that is not just isolated to the joint, but involves interplay between systemic factors and local (joint) factors.[1,3]

1.2.5 Epidemiology and natural history

The incidence of knee OA is around 160-240 per 100,000 person years, with the prevalence increasing with increasing age.[3] Approximately 20% of people over 40 have self-reported knee pain – half of these (10% of the population) can be expected to have radiographic changes consisted with knee OA.[3] For people over 60, approximately 15% have symptomatic knee pain with radiographic changes (30% of the population have radiographic changes in this population).[1]

Progression of knee OA is normally a slow process over the course of several years. Rates of progression reported in the literature vary greatly, confounded by follow up at different time points and the use of different diagnostic criteria (radiographic being the most common).[3,7] Table 1 demonstrates the rate of progression of knee OA from various studies.

Table 1: Natural history of diagnosed knee OA

Study	Number of subjects	Measure	Follow-up (years)	Proportion deteriorated (%)
Hernborg (1977)	84 knees	Clinical	15	55
		Radiographic	15	56
Danielsson (1970)	106 knees	Radiographic	15	33
Massardo (1989)	31	Radiographic	8	62
Dougados (1991)	353	Clinical	1	28
		Radiographic	1	29
Schouten (1991)	142	Radiographic	12	34
Spector (1991)	63	Radiographic	11	33
Spector (1994)	58	Radiographic	2	22
Ledingham (1995)	350 knees	Radiographic	2	72
McAlindon (1999)	470	Radiographic	4	11
Cooper et al. (2000)	354	Radiographic	5	22

Table reproduced with permission from Elsevier: Osteoarthritis: Epidemiology, Nigel Arden, Michael C. Nevitt, Best Practice & Research Clinical Rheumatology, February 2006.

In 2012 Leyland et al. reported a study that is not documented in the table above.[10] They reported the result of a 15-year follow up study using radiographic criteria. Participants were women aged 45 to 64 at baseline. The incidence of new OA knee was 40%, and the rate of progression varied from 10 to 70% depending on the baseline stage. Table 2 demonstrates a cross tabulation of results from this study – by far the largest with 15 year follow up.

Table 2: Cross tabulation of baseline and 15 year follow up radiological knee score. Chingford Study.

	K/L grade at year 15					
Baseline K/L grade	**0 n(%)**	**1 n(%)**	**2 n(%)**	**3 n(%)**	**4 n(%)**	**TKR at year 15**
0 (n = 955)	575 (60.2)	95 (10.0)	157 (16.4)	116 (12.2)	2 (0.2)	10 (1.1)
1 (n = 61)	12 (19.7)	4 (6.6)	24 (39.3)	18 (29.5)	0 (0.0)	3 (4.9)
2 (n = 76)	0 (0.0)	1 (1.3)	39 (51.3)	32 (42.1)	0 (0.0)	4 (5.3)
3 (n = 30)	1 (3.3)	1 (3.3)	4 (13.3)	19 (63.3)	3 (10.0)	2 (6.7)

K/L = Kellegran Lawrence classification
Reproduced with permission from Wiley and Sons: K. M. Leyland, D. et al., The natural history of radiographic knee osteoarthritis: A fourteen- year population-based cohort study, Arthritis & Rheumatology, Jun 26, 2012

Regardless of the diagnostic criteria it is clear that not all cases progress and a proportion of patients can expect either a halt in their progression, or an improvement in their symptoms (although radiographic improvement is rare).[3,10,11] The different clinical course for different patients is likely due to the various factors mentioned above.

1.3 Treatment of knee OA

There are generally accepted guidelines on the treatment of knee OA, and a summary is available in Figure 2.[2,12]

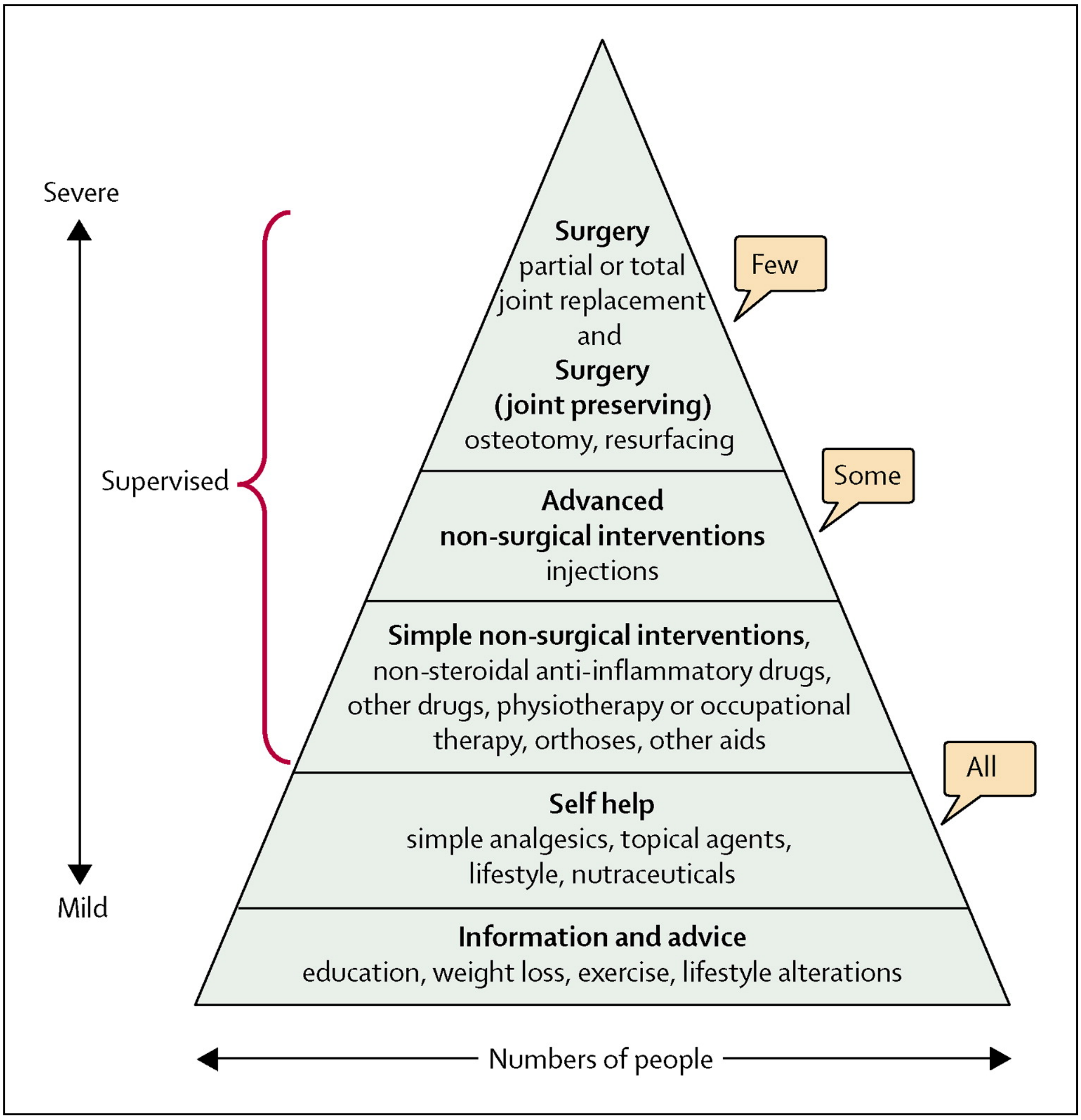


Figure 2: Treatment for OA
Reproduced with permission from Elsevier: Paul A Dieppe, L Stefan Lohmander, Pathogenesis and management of pain in osteoarthritis, The Lancet, 18 March 2005

For symptom control, core parts of treatment for early stage OA involve exercise, weight loss, and pain management. To try and reduce progression of the disease interventions are targeted at known risk factors – for example weight loss and addressing biomechanical factors (e.g. Anterior Cruciate Ligament (ACL) reconstruction). Potential future targets include aspects of the inflammatory response to microtrauma that drive the progression or facilitate the repair process (if such targets exist).[1]

Patients with increasingly severe symptoms may require surgery. There are a number of surgical options for patients with knee OA including:

- Osteotomy. This procedure aims to offload the damaged compartment of the leg, thereby relieving symptoms and slowing the progression of OA. It is therefore not suited to patients with both medial and lateral compartment OA. A recent Cochrane review noted that comparative studies between osteotomy and conservative care are lacking, but case series suggest osteotomy does relieve symptoms in a proportion of patients.[13] Good evidence on long-term follow up is lacking. Two recent Randomised Controlled Trials (RCTs) have compared osteotomy to unicompartmental knee replacement, with no difference in outcome noted, but higher (although not statistically significant) adverse events in the osteotomy group.[13]

- Cartilage repair/regeneration techniques. These techniques include microfracture and Autologous and Matrix-induced Autologous Chondrocyte Implantation (ACI and MACI). These techniques are only suitable for focal cartilage defects, predominantly on the femoral side.[14]

- Arthroscopy. Arthroscopy has been used for over 70 years in the treatment of OA knee. However, a landmark study by Moseley et al. comparing arthroscopy to sham surgery, combined with subsequent RCTs found arthroscopy was not indicated for OA of the knee.[15] This was reflected in NICE guidance in 2008 and again in 2014.[12] However, many arthroscopies are still performed: various reasons for this have been identified including the suspicion that some subgroups, not identified or included in the RCTs, may benefit (e.g. those with meniscal tears and mechanical symptoms).[15]

1.3.1 Knee replacement

A proportion of people go on to develop increasingly severe symptoms that affect their quality of life. For these patients, knee replacement is an option. However, there are no agreed criteria for patients to proceed from conservative management to knee replacement because the patient's preference plays a primary role (i.e. this is a preference-based decision).[16] This aspect of the patients' pathway is explored in chapters 2-4.

Knee replacement operations can be divided into unicompartmental knee replacements (namely the lateral and medial tibiofemoral compartments and the patellofemoral compartment), and total knee replacements.

Unicompartmental replacements are restricted to patients that have disease in only one compartment of the knee, and do not have instability of the knee. They have a good 10 year survival of over 90%, but this is not as good as total knee replacement.[17] Around 8% of the replacements performed in the UK are unicompartmental.[17]

Patellofemoral replacements account for a small percentage of replacement operations (around 2%). Indications include OA limited to the patellofemoral compartment of the knee. These replacements have a similar 10 year survival of around 10%.[17]

Total knee replacement

The first total knee replacement was performed by Theophilus Gluck in 1890 using an ivory hinge secured with plaster of Paris and resin.[18] The term "total" here refers to replacement of both medial and lateral compartments. It is not until 1970, 80 years after the first replacement, that more modern prostheses appear. These early designs generally had high failure rates. However, improvements in design have resulted in a 10 year failure rates of less than 5%.[17]

Total knee replacement may or may not resurface the patella, but always replaces both the medial and lateral tibiofemoral compartments and the femoral trochlea. In the U.K. almost 90% of knee replacements are total knee replacements.[17] There are many different types of total knee replacement (e.g. constrained versus unconstrained) and different methods of fixation. However, most modern total knee replacements appear to provide similar outcomes, and in the UK around 70% are fixed bearing cemented total knee replacements.[17]

The number of knee replacement operations undertaken in England and Wales has increased steadily. The National Joint Registry (NJR) demonstrates that currently over 90,000 knee replacements are performed each year in the NHS.[17] Projections on the number of knee replacements required in the future vary widely, primarily based on differing assumptions of population demographics and current trends in utilisation of total knee replacement. Current estimates vary by a 30% to a 1000% increase in demand by 2035.[19]

Although knee replacements are expensive costing around £6,500 per procedure, they are one of the most cost-effective interventions for any illness or disease, with recent estimates calculating they cost around £2,101 per Quality Adjusted Life Year (QALY).[20,21]

1.4 Problems facing knee replacement services

Although knee replacements are effective both in terms of cost and outcome, there are three problems facing the provision of knee replacements. First and foremost, there is a variation in the outcome – around 17% of patients are dissatisfied with the outcome of their operation, although estimates vary.[22,23] Secondly, and by no means specific to knee replacements, there is increasing demands coupled with financial constraints. Thirdly, there is a variation in the utilisation of knee replacements.

1.4.1 Variation in outcome

Questions have been raised about the benefits of knee replacements, and some studies report up to 17% of patients are dissatisfied with the outcome of knee replacement surgery.[17,22,24] The situation (regarding knee surgery in general) has been commented on by the Secretary of State for Health, who was reported to say in 2012:

"An interesting case in point is knee surgery; the data has now come back demonstrating half of knee surgery doesn't substantially change the outcome for patients: their mobility isn't improved that much, nor their pain."[25]

This comment was met with disappointment in the orthopaedic community, not least from the British Orthopaedic Association (BOA) and the British Association for Surgery of the Knee (BASK). They cited the words of a former BOA president that the Department of Health (DoH) uses data like "a drunken man using a lamppost, more for support than illumination".[25] Although these comments were widely regarded as misrepresenting the data, the fact remains that there is a significant group of patients that are dissatisfied with the outcome of their surgery, and that this has not gone unnoticed. Patients that are dissatisfied tend (unsurprisingly) to have worse Patient Reported Outcome Measures (PROMs) scores, such that they display worse pain outcomes and worse functional outcomes that those that are satisfied.[26]

A research prioritisation workshop on hip and knee replacement, sponsored by Arthritis Research U.K., the NJR, and the BOA, identified the question of '... which patients had poor outcomes and were dissatisfied...' as the most important research question in knee surgery today.[25] Additionally, the James Lynd alliance priority setting partnership, conducted in collaboration with the National Institute for Health Research (NIHR), has the identification of pre-operative predictors of success as one of its "Top Ten" research questions; and the National Institute for Health and Care Excellence (NICE) has stated that the development of methods to predict outcome in knee replacement is a research priority.[12]

1.4.2 Increasing demand with financial constraints

Currently the U.K. government has ring-fenced the NHS budget against the austerity measures imposed after the global financial crisis of 2008.[27] However, a King's Fund report into NHS performance revealed a £630 million deficit half way through financial year 2014/15.[27] They predict an additional £8 billion in funding will be needed each year by 2020. The present Conservative government has committed to meet this shortfall; however, the financial calculations are based on a £22 billion efficiency saving by 2020.[27,28] With efficiency savings as the goal for managing budgets within the NHS for several years, it is questionable if the NHS can meet its financial target (efficiency savings inevitable become harder year on year), and the King's fund has suggested that additional investment will be required to deliver essential changes to services.[27,28]

In any event, efficiency savings appear to be a key strategy to managing the ever-growing budget.[28] A more judicious use of knee replacement surgery, combined with the best possible conservative care, has potential to decrease the number of knee replacements performed (or slow the increasing numbers needed), and may go some way to relieving the financial pressure.

1.4.3 Variation in the utilisation of knee replacements

Variation in the utilisation of healthcare has been present within the National Health Service (NHS) for decades, and was the explicit reason for the establishment of NICE in 1998 (a move against the "postcode lottery").[29] Although hailed as a success at addressing healthcare inequalities, NICE has a limited role in guiding decisions over total knee replacement. NICE guidelines on the treatment of knee OA are available;[2] however, as knee replacement is a preference-based decision, no formal criteria have been agreed.[16] Indeed, the pathway from patients attending GPs, referral to orthopaedic services, and receipt of a joint replacement is inconsistent.[30]

The NHS Atlas of Variation describes knee replacement utilisation in different areas of the country.[31] Differences in expenditure of almost fourfold are demonstrated between Primary Care Trusts (PCTs) with regard to inpatient knee replacement costs; however, those Trusts with the highest expenditure reveal patients with the best pre-operative PROM scores. In other words those areas where there is objectively the lowest need (as measured by pre-operative PROMS) there is the highest rates of knee replacement – the so-called "Inverse Care Law". Some authors dispute the validity of assessing individual need based on PROMs;[25] however, the case remains that there appears a population level discrepancy in knee replacement utilisation.

In a recent systematic review, this variation in the utilisation of total knee replacement has been described by age, gender, race, education, income/health insurance (only studied in the USA), and employment.[32] Within the UK, the British Medical Journal (BMJ) reported that rates of knee replacement vary by age, gender, deprivation, rurality, and ethnicity. [33]

Warranted versus unwarranted variation

The NHS Atlas of Variation defines warranted variation as that explained by patient need or patient preference, and unwarranted variation as due to differences in access to healthcare and clinical practice.[31] Simplistically, this could be divided into demand (patient preference) and supply (access).

Recent studies have demonstrated that there is a marked warranted variation in knee replacement surgery. Only around one third of patients considered to be at need of a joint replacement would be willing to undergo a joint replacement.[34] Therefore patients' willingness to undergo a knee procedure will affect demand (and therefore affect geographical variations in utilisation).

Several studies have demonstrated that willingness to undergo a knee replacement varies by age, race, how OA is viewed (a natural process involved in getting older compared to a disease), and the amount of pain and disability that is required to justify the operation.[32,34] Furthermore, expectations of the outcome of the operation varies by gender, socioeconomic status and race.[35,36] Some differences in utilisation rates by race, age, income, but not gender have been explained by patient preference.[37,38]

These differences are key areas when considering developing prognostic models, as they demonstrate that expectations affect the willingness to undergo knee replacement operations, and that in turn may affect utilisation of knee replacements in a given population.

Within the U.K. it is clear that not all the variation is warranted (i.e. due to patient need or preference). For example, orthopaedic surgeons and general practitioners have been reported to be less likely to refer a woman with OA of the knee for knee replacement than a man (although more women actually have the procedure).[39]

Overall the factors that influence the variation in uptake of knee replacement surgery is likely to be a mixed picture of patient need, patient preference, access to healthcare, and clinical practice. Understanding how patients make decisions about having a total knee replacement could explain some of this variation.

1.5 Aims and objectives

Total knee replacement is a preference-based decision (i.e. it is done to improve quality of life, and the decision to proceed is therefore based primarily on the patient's preferences).[19] If the decision-making process surrounding knee replacement surgery could be improved, it should go some way to addressing the variability in outcome, the increasing demand, and the variation in utilisation.

Therefore, this thesis has two aims:

1. To understand which factors affect patient decision-making when considering a knee replacement, and how prediction of outcome could affect patients' decision-making process. This will answer the following questions:

- What factors are important in patient decision-making?
- Would information on a likely outcome alter patient expectations?
- Would information on a likely outcome alter patients' decision-making process?
- What sort of information would be most useful to patients (e.g. a prediction of their OKS score, or a predicted chance of satisfaction)?

Chapters 2, 3, and 4 describe a systematic review of the factors that influence patient decision-making, and report a qualitative study examining both the factors that effect patient decision-making, and the effect a fictitious outcome prediction tool may have.

2. To develop a prognostic model that could be used to help the decision-making process for patients' considering knee replacement surgery. To do this the following objectives need to be met:

- Identification of the important pre-operative factors
- Development of a cohort study to measure those factors in patients receiving a knee replacement
- Statistical modelling to develop an algorithm for predicting post-operative outcomes in patients.

Chapters 5, 6 and 7 describe a systematic review identifying the important pre-operative factors, the subsequent protocol for a multicentre cohort study of 600 patients measuring all of the important pre-operative factors, and the conduct of that study with the final prognostic model.

Critically, this body of work aims to develop a new prognostic model that can predict more variability in outcome than previous attempts. Although the usefulness of the model produced is discussed, the process of preclinical development and impact evaluation, which are critical steps in the development of an outcome prediction tool, does not form part of this thesis.

1.6 Potential implications of this work

A prognostic model may prompt investigation into modifying patient factors that are associated with poor outcome. Patients' functional and pain outcomes may be improved by modifying these factors (e.g. using Cognitive Behavioural Therapy to alter coping strategies).

Identifying important pre-operative factors related to outcome could also prompt future work in case-mix adjustment. This is especially relevant given the recent publication of individual surgeons' outcomes (although currently related to mortality), and the recent decision to base the Best Practice Tariff for hip and knee replacement partly on a case-mix adjusted PROM score.[40]

A prognostic model is also the first step in the development of an outcome prediction tool. Such a tool, used in conjunction with a surgeon's normal pre-operative counselling, may alter patients' decision-making process. For example, some patients who have been offered knee replacement may elect not to have operation based on predictions of poorer outcomes (going some way to address increasing demand). Additionally, patient's expectations may be altered with outcome prediction, and therefore their satisfaction could improve (i.e. those patients with poorer predictions would expect poorer outcomes). There is conflicting evidence linking pre-operative expectation and post-operative satisfaction in knee replacements, potentially due to difficulties in measuring these constructs;[41] however, a relationship is logically consistent.

Chapter 2. Decision-making models and patients' decision-making in total knee replacement

A patient-centred approach, usually achieved through shared decision-making, has the potential to help improve decision-making around knee replacement surgery. However, such an approach requires an understanding of the factors involved in patient decision-making. This chapter examines models of decision-making in the NHS and presents a systematic review of the qualitative literature surrounding patients' decision-making in knee replacement surgery, identifying the factors that affect patients' decision-making.

2.1 Declarations

Aspects of this chapter have been published:

T. Barlow, D. Griffin, D. Barlow, A. Realpe. Patients' decision-making in total knee arthroplasty. A systematic review of qualitative research. Bone and Joint Research. 2015;4:163–169.

Dr A. Realpe provided independent data extraction. Dr D. Barlow provided independent assessment of references for inclusion.

2.2 Introduction

Understanding patients' decision-making has the potential to improve the information given to patients (particularly probabilistic predictions of outcomes), to enhance patient-centred care, and to inform patient decision aids.[42] Improved pre-operative counselling could help address the three problematic areas facing knee replacement services: (i) a high dissatisfaction rate; (ii) increasing demand with financial constraints; and (iii) a variation in the utilisation of knee replacements.[42]

Decision-making within medical practice is an area that has been intensively studied as it is recognised to play a key role in medical interventions.[43] There are several models of decision-making, each with its own advantages and drawbacks.[43] Associated with these models are interventions, directed towards both physicians and patients, aimed at helping the decision-making process.[44,45] It is necessary to understand this background before the intricacies of decision-making in knee replacements are explored. This chapter is therefore split into two parts:

- Section 2.3 Decision-making models in the NHS: trends over time, and the evidence base for favouring one approach over another.
- Section 2.4 Systematic review of current knowledge of decision-making in knee replacements.

Before moving on to discuss decision-making models, it is important to recognise that knee replacement surgery is a preference-based decision: this means that the patients' decision to progress to knee replacement is based on their preferences (along with the surgeon's assessment that it is a suitable option). With the ultimate aim of understanding what is currently known about decision-making in knee replacements, preference-based decisions form the basis of the literature reviewed here.

2.3 Decision-making models in the NHS

There are many descriptive models based around the delivery of health care. For the purposes of this review, I deal with three models: the paternalistic, the shared decision-making, and the informed models.[43]

The paternalistic model of delivery of healthcare (occasionally termed the traditional medical model) was historically the prevalent method of delivering healthcare.[43] This involved an interaction where the clinician chooses the therapy he or she deems to be best. The patient is a passenger within this process. In contrast stands the informed medical model in which the clinician supplies information on the various treatments available and lets the patient decide.[43]

Shared Decision-making sits between the paternalistic and informed models in that there is a transfer of information between clinician and patient, and a decision is reached together.[43] It has been defined as:

" A process in which clinicians and patients work together to select tests, treatments, management or support packages, based on clinical evidence and the patient's informed preferences. It involves the provision of evidence-based information about options, outcomes and uncertainties, together with decision support counselling and a system for recording and implementing patients' informed preferences".[46]

As such, the shared decision-making model uses evidence based medicine (prevalent in the paternalistic model) combined with a patient-centred approach.

One method of deciding on which decision-making model to use between doctor and patient is to determine how involved patients want to be in medical decision-making. A systematic review by Say et al. demonstrated that patient preference for involvement in medical decisions was influenced by age, gender and education, with young, female, well educated patients having a preference for more information.[47] Further factors that have been identified are more complex, and include patients' experience of medical care, co-morbidity, diagnosis, type of decision, and interaction with health professionals.[47,48] It is also clear that a patient's preference for involvement changes at different stages of their illness.[48] Although relevant to preference based decision-making, no specific studies on preference have been conducted in elective knee replacement surgery.[48]

Therefore patients' preferences for information and involvement in medical decision-making are varied and complex, and different models may be more appropriate than others in different situations. Attempts at predicting patients' preferences for involvement in decision-making have so far been unsuccessful, due in a large part to the complex nature of the topic.[49] This leads to the question of which model to use primarily, and are there other ways of selecting that model (e.g. based on health outcomes)?

2.3.1 Shared decision-making and Patient Decision Aids

Within the NHS there has been a move towards a "Shared-decision" making paradigm, which has been promoted in the slogan "No decision about me, without me".[46] Although this model might not serve all patients all the time, a Department of Health White paper has committed the NHS to ensure that "Patients will be in charge of making decisions about their care" and "Shared decision-making will become the norm".[28]

Accompanying this political drive, NICE has released quality standards supporting this philosophy stating that patients should be "actively involved in shared decision-making" [50]

Why use the shared decision-making model?

This is based on three principles:

Firstly, some authors have demonstrated that many patients (as much as 94% in some settings) want more information about decisions. [47] A desire for more information does not mean a desire for involvement in decision-making *per se*, although the two have an association. [47]

Secondly, the ethical principle of autonomy has resulted in shared decision-making being part of the ethical guidelines for clinicians.[51]

Thirdly, there is evidence that a patient-centred approach facilitates patient experience and health outcome. This evidence can broadly be divided into two categories: interventions for providers, and interventions for patients.

Interventions for providers

A recent Cochrane review examined 43 randomised controlled trials of interventions aimed at improving patient-centred consultations.[44] A range of measures were examined, and in general interventions (primarily training sessions for providers of healthcare) showed positive results on "clarifying patients' concerns and beliefs; communications about treatment options; levels of empathy; and patient perception of providers attentiveness to them". Furthermore, the authors analysed health outcomes. Here there were mixed effects. Most relevant to knee OA, studies with complex interventions using condition specific materials generally demonstrated an improvement in health behaviour and satisfaction. The only orthopaedic study included in the review involved training General Practitioners in consultation with patients. Those patients who received care from patient-centred-trained GPs had improved pain, improved PROM function, and a better perception of treatment.[52] However, a similar study showed a conflicting result; a randomised controlled study conducted at Warwick University found worse health outcomes for patients with low back pain treated by providers trained in shared decision-making.[53].

Therefore, shared decision-making on the part of the provider may have positive results on how a patient feels about the treatment, but it is unclear whether it is helpful or detrimental to the health outcome.

Interventions for patients

Patient Decision Aids (PDA, also known as decision aids, decision support interventions, decision support aids) are methods of informing patients about the treatment options available to them. From a simple one-page summary to interactive online tools, they have been widely implemented within the NHS, with the Department of Health Quality, Innovation, Productivity, and Prevention (QIPPs) programme funding the development and hosting of 38 PDAs to cover a variety of conditions. Knee OA is included.[46]

A recent Cochrane review on the effectiveness of decision aids [45] concluded that in general:

- Patients' knowledge of the options improve (high-quality evidence);
- Patients feels more informed and more clear about what matters most to them (high-quality evidence);
- Patients have more accurate expectations of possible benefits and harms of their options (moderate-quality evidence); and
- Patients participate more in decision-making (moderate-quality evidence).

Interestingly decision aids have been found to reduce the proportion of people progressing to elective surgery.[42,45] Although these studies did not involve patients with knee OA, there are clear parallels with other preference-based decisions[42]

Currently the International Standard Randomised Controlled Register (ISRCTN) has one registered trial examining the effect of a PDAs in knee OA.[54] This trial in ongoing.

A complicating factor, mentioned in both the Cochrane review and a review of PDAs in orthopaedics, is the varying quality of PDAs.[42,45] Guidelines for the development and evaluation of PDAs have been developed in response to this.[42]

Summary

A shared decision-making approach in knee replacement surgery is consistent with ethical guidelines, there is evidence that a proportion of patients would prefer it, it leads to better patient satisfaction with the interaction, it is consistent with current political targets, and it is appropriate to a preference-based decision. However, several caveats exist: these include the complex nature of patient preference towards the amount of information; patient preference for involvement in decision-making; and concerns over the quality of some PDAs. But perhaps the largest concern is the unknown effect on health outcomes.

However, shared decision-making appears to be a useful method and may go some way to addressing some of the problems that clinicians are currently facing in knee replacement surgery – namely limited resources with increasing financial pressure, a significant dissatisfaction rate, and wide variation in utilisation.

Shared decision-making in knee replacements requires a firm understanding of the process involved in patients' decision-making, and the factors that affect that process. Understanding patients' decision-making process will also directly help understand variations in the warranted utilisation of knee replacements.

2.4 Systematic review of factors that influence patient decision-making in knee replacements.

2.4.1 Background

An understanding of patients' decision-making will be helpful not only in enabling high quality, patient-centred interactions, but in highlighting areas that future interventions could address (particularly interventions aimed at delivering information).

Various attempts at identifying how patients make decisions about knee surgery, and what factors are important to them, have been conducted. Interestingly, many studies have examined both hip and knee patients as one cohort. Additionally, historic attempts at synthesising the qualitative literature on this topic have likewise included both hip and knee patients as one patient group.[55] Although there are clear similarities between these groups, there are significant differences that make combining these populations potentially unsound.

Firstly, there is the significant difference in the "success" rate of hip and knee replacements. Total knee replacements have a dissatisfaction rate of around 17%.[25,56] Hip replacements have significantly better outcomes as regards satisfaction, pain, and function.[57] Ibrahim et al. examined the influence of expectations as an explanatory factor in some of the variation in utilisation rates of joint replacement, and found that it explains some of the variation.[35] Therefore, knee replacement decision-making (associated with utilisation) is likely to be different to that for hip replacements, as the outcome is not the same.

Secondly, the population that develops hip OA is different to the population that develops knee OA. A recent study including almost 2000 participants found that BMI was correlated with the development and progression of knee OA, but not hip OA.[58] This is particularly relevant to decision-making, as people with higher BMIs display different psychological profiles to the general population.[59]

Therefore people who develop hip and knee OA are likely to be different populations, with different psychological profiles. Additionally, the outcome, and therefore expectation, of the operations are different.

2.4.2 Aim

In this review I aggregate the qualitative literature surrounding patients' decision-making in knee replacement surgery. The aim of this review was to provide an aggregation of studies (cf. a synthesis of qualitative studies). The difference is accumulation and summary, rather than transformation.[60] This represents an approach consistent with a "lines argument synthesis", defined as "building up a picture of the whole" and represents what has been described in the literature as a realist synthesis with narrative review;[61] however, the term synthesis here refers to the combination of results, rather than any second or third order interpretation from them.

2.4.3 Methods

I conducted a literature search of Medline and Embase in January 2015. Subject and topic terms (Knee, Knee prosthesis, Knee replacement, Knee arthroplasty and Decision-making) were included, both as free text and indexed headings. I conducted a bibliographic search of all studies retrieved for full text analysis (whether included in the final review or not). English only articles were included. This search strategy is consistent with that used by the Evidence for Policy and Practice Information Centre.[62]

Studies that reported qualitative data on the decision-making process in knee replacements were included. I selected the relevant papers, and conducted a bibliographic search. All full text papers retrieved were screened by a second author (DB) to provide consensus that papers were reporting qualitative findings on decision-making. We did not specifically exclude survey data; such papers were required to provide insights into decision-making over-and-above reporting descriptive or inferential statistics. The eligibility criteria were:

Inclusion:

- Findings on how and why patients make decisions regarding knee replacement
- Recognised as qualitative research

Exclusion

- Knee patients' decision-making not reported separately

Consistent with most authors conducting aggregations of qualitative work, quality assessment was not performed.[62,63]

There exist many different methodologies for the synthesis of qualitative work. These differing approaches are in some part due to the prolific use of modified techniques, compounded by inconsistent and confusing nomenclature[64,65] A common issue surrounds the terms synthesis itself: many authors suggest this includes a transformation of the data contained within the original studies (i.e. new insights or frameworks, based upon the original studies but not necessary contained within them).

However, my aim here was not to synthesise the studies in this sense, but to provide a map, or a picture of the whole. This is consistent with approaches described in the literature.[60-62,64,65] This approach involved identifying themes that the authors of primary studies had recognised as important to decision-making. Themes and, where appropriate, sub-themes are reported as per the authors' classification. Therefore the authors' own findings, in their own words as far as possible, are reported, and any clear consistencies or inconsistencies are discussed. I completed this process, and the findings were crosschecked by another experienced qualitative researcher (AR).

2.4.4 Results

The electronic database search returned 556 papers. Seventy papers remained after a title review, and a further 50 papers were excluded on the basis of their abstracts. A further 11 papers were retrieved for full text review from the bibliographic search (a total of 31 papers for full text review). Of these, seven were included in the review. A flow diagram of the included papers is displayed in Figure 3.

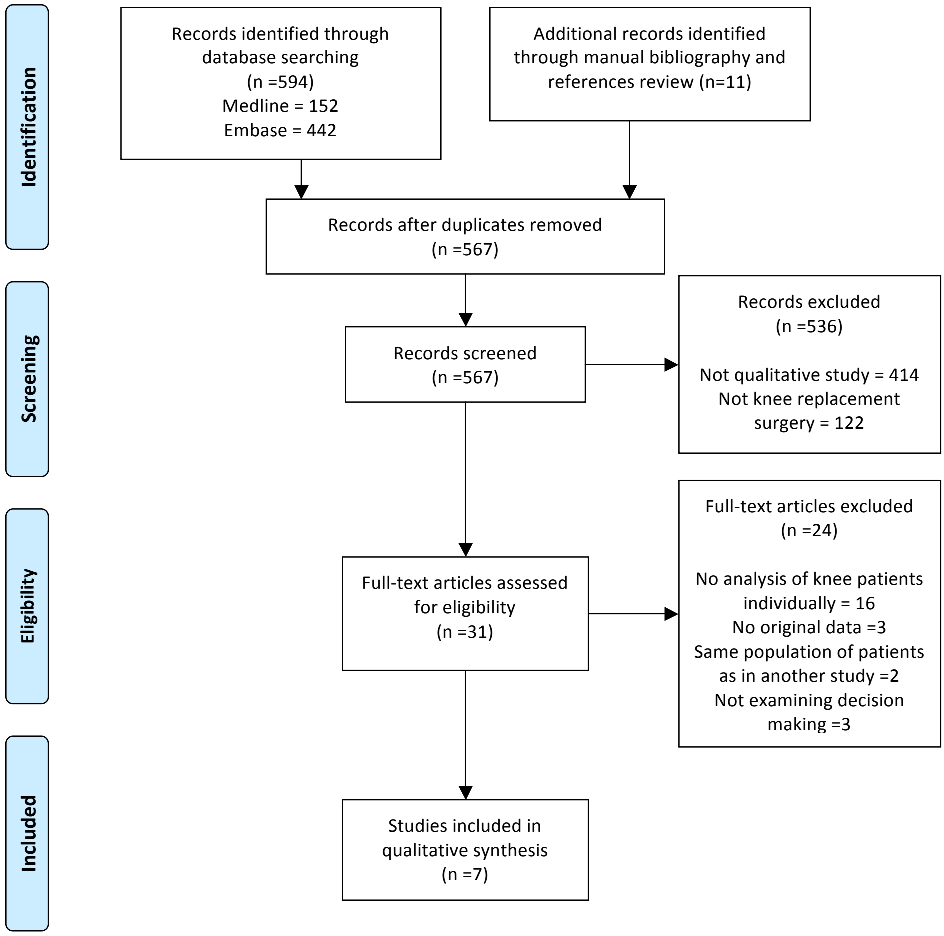


Figure 3: PRISMA flow chart of included studies. Adapted from Moher et al.[66]

Study characteristics

Studies have examined decision-making in a population with knee symptoms but no diagnosis of knee pain,[67] patients in primary care with a diagnosis of knee OA,[68] patients actively considering a knee replacement in secondary care,[69] patients on the waiting list for knee replacement,[70-72] and recent post-operative patients.[73] Of note, two papers had a focus that was not decision-making in knee replacements; however, some themes were relevant so both papers were included.[72,73]

From the seven studies, four different countries are represented with 234 participants. Study samples range from nine to 94 participants (average 33 participants). One hundred and twenty-six of the 234 participants are African American (skewed by one large study of 94 participants)[67], with 39 Kuwaiti women, 33 “white” or “white American”, nine European New Zealanders, with two studies (43 participants) not reporting ethnicity. Sixty-eight of the 234 participants (29%) were male. Three studies conducted focus groups, with four conducting interviews. Analysis was reported in a variety of ways, with different nomenclature. Study characteristics can be found in Table 3.

Table 3: Basic study characteristics (continued overleaf)

Author	Title	Setting	Sampling	Participants	Method	Analysis
Figaro et al.	Preferences for Arthritis Care Among Urban African Americans: "I Don't Want to Be Cut".	Church or senior centre in Manhattan, New York, USA.	Opt in recruitment from patients who had pain or stiffness in one or both knees.	94 African American/Black participants. (79 female, 15 male). Mean age 71. 82 without and 12 with a knee replacement.	Structured interviews	Content analysis using constant comparative method.
Suarez-Almazor	A qualitative Analysis of Decision-Making for Total Knee Replacement in patients with OA.	Primary care setting in USA.	Patients identified as sub-population of another study, with a diagnosis of knee OA but no TKR.	37 patients. 13 white, 9 Hispanic, 15 African American. 14 males, 23 females. Mean age 64.	Focus group	Thematic analysis using a grounded theory approach.
Chang et al.	Concerns of Patients Actively Contemplating Total Knee Replacement: Differences by Race and Gender	Orthopaedic surgeon's office. USA	Patients actively considering a knee replacement. Patients were recruited in sequence of attendance.	12 male, 25 female. 20 white American, 17 African American. Mean age 60.	Focus group	Thematic content analysis
Al-Taiar et al.	Attitudes to knee OA and total knee replacement in Arab women: a qualitative study.	The only Publicly funded orthopaedic centre in Kuwait	Patients selected from the waiting list for knee replacement. Process not reported.	39 Kuwaiti female participants. Mean age 62.5.	Semi-structured focus group	Thematic analysis

Table 3 (cont.)

Author	Title	Setting	Sampling	Participants	Method	Analysis
Toye et al.	Personal meanings in the construction of need for total knee replacement surgery.	Specialist orthopaedic centre, England, UK.	Patient on waiting list for TKR and below average need as judged by WOMAC pain and function score. Invited by letter (opt in).	18 patients (12 male, 6 female). Average age and ethnicity not reported.	Semi-structured interviews	Interpretive phenomenological analysis.
Woolhead et al.	Who should have priority for a knee joint replacement?	Three orthopaedic surgeons' waiting lists, UK.	Patients on the waiting list for knee replacement. Sampling across age and gender by letter (opt in).	25 participants (14 female, 11 male). Mean age 65.	Semi-structured interviews	Constant comparison
Marcinkowski et al.	Getting Back to the Future. A Grounded Theory Study of the Patient Perspective of Total Knee Joint Arthroplasty.	A publically funded centre in New Zealand.	Purposive sampling by age, gender, comorbidity and complications from patients who had recently had a knee replacement.	9 European New Zealand participants (4 male, 5 female). Mean age 71.	Unstructured interview.	Constant comparative analysis based in grounded theory

Study themes

A matrix of study themes has been produced (Table 4), demonstrating where themes overlap, and where they do not. The description of themes is taken from the relevant papers, but summarised where necessary. As described in the methods section, no transformation of the data took place.

Expectation of surgery was a theme identified in five of the seven studies.[67-71] A common finding was the uncertainty surrounding the outcome of a knee replacement.

Four studies identified various patterns of coping mechanisms, which were important in the decision-making process.[67,70,71,73] The use of alternative medicine and social support was prevalent. Two studies identified religion as part of the preferred coping mechanism.These mechanisms may help people live with OA and therefore predominantly act as deterrents to operative intervention; however, they can also act as stimulators (e.g. social support in helping to make the decision).

The relationship with the clinician was recognized as important in four studies. This was almost universally seen as a major factor in decision-making; however, one paper found that trust in physicians was not an important factor in decision-making. Related to this theme, two papers documented the role of "decisional conflict" in decision-making. Woolhead et al., who examined patients' views on prioritisation for surgery, found that decisional conflict existed due to differences of opinion between patient and surgeon.[72] This was consistent with finding from Suarez-Almazor.[68] Interestingly, patients in these studies interacted with both primary care physicians and surgeons, suggesting conflict can continue throughout the patients' journey to knee replacement.

Many fears were identified in the studies. Common fears were that of the operation (with associated anaesthesia), recovery, and outcome. One fear was related to another theme: pain (predominantly pre-operative pain). Pain was identified in four of the studies, with the effect on participants' life being a major factor in decision-making.

Function (both poor functioning pre-operatively and expected good functioning post-operatively) was reported in three studies as a decision-making factor.[70,71,73] Some authors included function with another domain (e.g. Marcinkowski et al. describe physical and emotional struggling as a theme). [73]

Psychological aspects (predominantly emotional) were explored in three papers.[70,71,73] The findings were quite consistent across papers involving participants that were on the waiting list, or that had received knee replacements. Feelings of frustration, vulnerability, letting others down, and self-image were discussed.

Patients' social network functioned both as a source of perceived pressure and as an information source related to the social networks' experience of surgery.[68,71] Related to this was a personal experience of surgery, identified by two studies.

Six further themes were identified by only one study. These included: surgery as a last resort, preference for continuing their current state, financial issues, different sources of information, and different preferences for participation in decision-making.

Table 4: Study themes (continued until page 43)

Summary theme	Figaro et al.	Suarez-Almazor	Chang et al.	Al-Taiar et al.	Toye et al.	Woolhead et al.	Marcinkowski et al.
Expectations of Surgery	**Negative expectations of Knee replacement.** Expectation that surgery "doesn't last" is a "last-resort", or that it introduces something "foreign" into the body.	**Expectations about improved function.**	**Post-operative.** Concerns included: benefits from surgery; long term outcome; recuperation process; function after surgery; quality of life after surgery; pain after surgery; methods of pain relief; support after surgery	**Expectation of knee replacement.** Varied, poor, and non-specific expectations were noted.	**Expectations.** Knee replacement seen as a "cure" with the expectation of an improvement in pain and function.		
Coping mechanisms	**Preference for natural remedies.** OA seen as a natural part of ageing. Desire to keep their body intact and the use of natural remedies. **Belief in God's control.** Over their health and eventual death.			**Impact of pain and/or mobility limitation upon family.** Family support a critical factor in coping with pain See also **Pain Experience and impact of knee pain on patients.**	**Dependency.** On family and friends.		**Seeking comfort.** Alternative medicine and medication.

Table 4 (cont.)

Summary theme	Figaro et al.	Suarez-Almazor	Chang et al.	Al-Taiar et al.	Toye et al.	Woolhead et al.	Marcinkowski et al.
Relationship with clinician	**Relationship with Specialist.** TKR was viewed as rarely offered, and therefore a last resort. Wary of having a knee replacement if they had experience of doctors laughing, yelling, or rushing them to make a decision.	**Relationships with doctors**. Especially trust, information, and communication.		**Process of decision-making to undergo knee replacement and pathway of care**. Feeling that knee replacement is offered once knee is "totally destroyed"; lack of information; trust in doctor not identified as an issue	**Medical Model.** A belief that medical diagnosis (confirmed on radiograph) determined need for knee replacement (and therefore determined by the doctor); Faith in the doctor as "expert" - although not absolute or 100% consistent.		
Fear	**Fear of surgery or death.** Fear and distrust of the medical system. Fear of a bad outcome from surgery	**Fears.** Length of recovery, fear from complications, anaesthesia, longevity of prosthesis, effect on co-morbidities.	**Intra-operative.** Concerns included Technique and anaesthesia	**Process of decision-making to undergo knee replacement and pathway of care.** Fear of the operation, anaesthesia, post-operative pain, poor outcome;			

Table 4 (cont.)

Summary theme	Figaro et al.	Suarez-Almazor	Chang et al.	Al-Taiar et al.	Toye et al.	Woolhead et al.	Marcinkowski et al.
Pain			**Pre-operative.** Various concerns raised including: alternatives to knee replacement; pain relief and addiction; lifespan of prosthesis; timing of knee replacement; employment; finance; trust in physician; anatomy; types of device; drawbacks to surgery; candidate for surgery	**Pain experience and impact of knee pain on patients**. Pain affected all aspects of life; pain management included medicine and alternative therapies; fear over side effects and addiction to medications prevalent; the cause of OA was important to patients; some participants turned to religion to help cope.	**Pain.** Important factor in determining need; however difficult to describe.		**Hurting.** Pain interfered with everyday activities and sleep.
Function				**Mobility limitation and the need for assistance**. Affected activities of daily living; fear of falling was common; feeling of failure and less value with regards their obligation towards family.	**Functional Loss.** With respect to walking shopping and leisure activities. Functional expectations decreased with age, reducing the perceived need for knee replacement.		**Struggling.** Physical and emotional struggle (coming to terms with how others viewed them and their own self image)

Table 4 (cont.)

Summary theme	Figaro et al.	Suarez-Almazor	Chang et al.	Al-Taiar et al.	Toye et al.	Woolhead et al.	Marcinkowski et al.
Psychological implications				**Mobility limitation and the need for assistance**. Affected activities of daily living; fear of falling was common; feeling of failure and less value with regards their obligation towards family.	**Vulnerability**. Physical vulnerability related to the knee "letting me down". **Low mood and fatigue**. Various psychological effects identified including frustration, fatigue, and depression.		**Struggling.** Physical and emotional struggle (coming to terms with how others viewed them and their own self image)
Social network		**Personal Experience.** Experience of relatives, friends and acquaintances played a major role			**Social Network.** As an information source, and a source of pressure to proceed.		
Previous experience of surgery		**Previous personal experience of surgery**. (Including non-orthopaedic surgery)		**Past Medical Treatment**. Pathways of care involved may different doctors in many different countries and led to a perceived overuse of medications and a delay to knee replacement			

Table 4 (cont.)

Summary theme	Figaro et al.	Suarez-Almazor	Chang et al.	Al-Taiar et al.	Toye et al.	Woolhead et al.	Marcinkowski et al.
Conflict in opinions		**Conflict in opinions.** Conflict between patients, families and doctors led to dissatisfaction.				**Decisional conflict** between how patients perceived prioritisation does happen and should happen (and whom doctors offer knee replacements to)	
Themes that are not replicated across studies	**Preference for continuing their current state.** Fear of the operation, unwillingness to make a choice that increases the risk of death, uncertainty about outcome, and satisfaction with their current lifestyles all featured.	**Surgery as a last resort.** Also referred to as a "Threshold for decision-making". **Financial issues.** Although this was a concern it was not seen as an insurmountable barrier to knee replacement. **Different sources of Information.** Primary care physician most common source of professional and medical information **Different preferences for participation in decision-making**			**Disease Progression.** Belief that the disease would progress, with consequences for later life.		

Table 4 (cont.)

Summary theme	Figaro et al.	Suarez-Almazor	Chang et al.	Al-Taiar et al.	Toye et al.	Woolhead et al.	Marcinkowski et al.
Comments	Overarching theme of preference for non-surgical treatment and apprehension: “I don’t want to be cut.”		Study was primarily aimed at identifying patient concerns over knee replacement	Trust in surgeon and concern over healthcare costs were not identified as concerns of patients.	Important to identify patients’ personal meaning during a clinical consultation to effectively collaborate on treatment decisions.	The paper focused on prioritisation for surgery. However, it found patients perceive a conflict between patients and doctors on how this process works, and the process of listing for knee replacement	This paper was a review of patients’ whole experience. It did not focus on decision-making, but did include some themes that were relevant.

2.4.5 Discussion

I have described a heterogeneous group of studies examining the decision-making process of patients when considering a knee replacement. Some themes are remarkably consistent; others have only been demonstrated in specific samples of patients. One theme, the relationship with the treating physician, was not found to be important in one study, contrasting with it being a major factor in four other papers. It may be this is a result of the study samples: the study that found this theme was not important included patients that had been seen by many doctors in many different countries.

The themes identified within this review are consistent with the wider literature of knee replacements. Huduk et al. investigated a population of patients with hip and knee OA who had elected not to have a replacement.[74] Patients that do not proceed to joint replacement tend to view OA as an inevitable part of ageing, see others as worse off than themselves, and wait for the doctor to recommend it. These finding are consistent with findings from our review, especially with the samples of patients who were earlier in their treatment course. This aspect is key in understanding the high rate of patients who are unwilling to consider knee replacement.[34]

Elwyn et al. suggested that the decision-making process can be split into deliberation and decision-making (also called determination).[75] This would suggest that the deliberation process occurs until the decision to have surgery is reached (what Clark et al. refer to as the "Decision-making Threshold").[76] Included studies demonstrated that patients experience decisional conflict; however, it is unclear if this conflict causes a degree of stress during the deliberation stage, or if this is resolved once the threshold is reached. It is also unclear if patients would be willing to move back into the deliberation phase if their symptoms improved. The relationship between the decision-making threshold and the movement from deliberation to decision-making is currently poorly understood, and is explored in chapters 3 and 4.

In 2007 O'Neill conducted a qualitative meta-sythesis of decision-making in joint replacement.[55] This concluded that social and cultural categories shape patients' expectations of treatment options. Coping strategies and life context determined the short and longer-term outcomes of joint replacement. Interestingly the strongest theme identified was trust in the health professional. This is broadly consistent with the findings of this review; however, one paper reports a notable exception.[70]

In 2012 Jayadev conducted a review on Patient Decision Aids.[42] This included evidence from a Cochrane review that concluded decision aids improved patient knowledge, resulted in less decisional conflict, less indecision, and greater concordance between patient values and chosen options. However, it also commented on the varying quality of decision aids, finding that the content regarding different treatment options was commonly lacking. Compounding this, our review would suggest that there are various concerns that patients have over and above the different treatment options (e.g. the "relationship with clinician"). Using the findings from this review, there is the potential to tailor the information in decision aids to address patients' major concerns.

This review is prone to various weaknesses. The indexing of qualitative work from electronic databases is not as well developed as that of quantitative studies.[64] Currently, there are no registers of qualitative work and qualitative studies commonly use descriptive or imaginative titles, making identification through standard search techniques problematic.[62,64] To address this, I used a broad based approach, searching for only the subject and topic terms.[62] This produced a large number of irrelevant studies, and, with an estimated 23% of studies not having indexed abstracts, resulted in a large number of full text articles being screened.[62] Furthermore, I conducted a comprehensive bibliographic search of all full text articles retrieved, including those excluded from the review. This approach is consistent with that used by the Evidence for Policy and Practice Information Centre.[62]

The definition of a qualitative study is problematic, with experienced qualitative researchers disagreeing over what constitutes qualitative research.[62] I addressed this by only including research that, in my and DB's opinion, was unequivocally qualitative in nature. Studies examining knee replacement decision-making with other conditions (e.g. hip replacement or back pain) were excluded.[55,77,78] These studies may have contained useful information, but were excluded on the basis that the themes might not have been relevant to knee replacement decision-making.

No synthesis of the data took place, although common themes have been highlighted. My aim was to provide an overview of what is know about how patients make decisions, and let the reader interpret the themes expressed from each paper.[61,62,64]

Various weaknesses were present in the studies included within this review. Some samples of patients were homogeneous within certain characteristics (e.g. black Americans).[67] Additionally, the stage of the decision-making process has not been addressed, with each included study focusing on one stage of the pathway of care (although Figaro et al. did include some post operative patients within their sample, it represented a very small number). The stage of decision-making is likely to be key to understanding the decision-making process, and therefore these studies lack an essential dimension. An interesting finding was that reporting positive findings (i.e. themes that were important to patients) was ubiquitous throughout all studies; however, only one study mentioned a negative result (i.e. a theme that was not important).[70] It is unclear if authors did not report negative findings, or did not make any attempts to investigate certain factors that could affect decision-making. This could be thought of as a reporting bias. To what degree this influenced the result is unclear.

It is also unclear from this work how individual prediction of outcome could affect decision-making.

The strengths of this study is the systematic method of identifying studies, the accurate reporting of themes from individual papers, and the process of validating the themes that were extracted from the papers.

2.4.6 Conclusion

I identified 17 individual themes across seven studies that covered all stages of the decision-making journey, from developing symptoms through to recovery after knee replacement. Ten themes were repeated across studies, with fear, pain, coping mechanisms, expectations of surgery, and the relationship with the clinician seen most frequently.

Understanding all facets that may affect patient decision-making when considering a knee replacement is essential to the shared decision-making process. This work can act as a framework for understanding common concerns of patients considering a knee replacement, in order to aid clinicians in delivering patient-centred care. Other methods of delivering information to patients (e.g. PDAs) should address these factors; however, how best to integrate these findings into information delivery systems for patients is an area that requires greater understanding.

By facilitating the patient-doctor interaction, a sound understanding of patient decision-making has the potential to address increasing financial pressures, variation in uptake, and improved satisfaction from surgery. However, this review is unable to provide us with a model of decision-making that is theoretically grounded, and is also deficient in that individual studies did not include patients at different parts of the decision-making process. The following chapter aims to address these limitations.

Chapter 3: A qualitative study on the factors affecting patients' decision-making in knee replacement.

This study uses focus groups and in-depth interviews to examine the factors that affect patient decision-making. I describe nine themes that affect patient deliberation over a decision. I base my findings in a theoretical model, proposed by Elwyn et al., that highlights the distinction between deliberation and decision-making, and add to this model by demonstrating the boundary between deliberation and decision-making is the decision-making threshold. This provides a model of decision-making for patients considering a knee replacement.

3.1 Declarations

Aspects of this chapter have been presented at an international conference:

T. Barlow, P. Scott, D. Griffin, A. Realpe. What factors affect patient decision-making in knee replacements? 23rd annual meeting of the European Orthopaedic Research Society.

This study was approved by the Dyfed Powys Research Ethics Committee (13/WA/0140).

Dr A. Realpe provided independent cross checking of thematic framework. Mrs P. Scott facilitated in focus groups, interviews, and analysis of qualitative data. An external company conducted transcription of focus groups and interviews.

3.2 Background

In the previous chapters the importance of understanding knee replacement decision-making was explored. This was focused around three key areas: differences in utilisation rates;[31] a high dissatisfaction rate;[25] and increasing demands with financial constraints.[27] How decision-making could have an influence on each of these factors was discussed.

Previous investigations have focused on populations at a different point along the treatment pathway. No previous study has included patients at different stages along that pathway, focusing instead on those with symptomatic knee problems,[67] considering a knee replacement,[69] on the list for a knee replacement,[70-72] or those who had already had a knee replacement.[73] The point on the pathway is likely to be important in decision-making, and therefore previous studies lack an essential dimension, providing only a "snap shot" of the decision-making process.

An understanding of patients' decision-making is critical in informing patient-centred care. It is also be helpful in understanding how an outcome prediction tool could affect decision-making.

Therefore our aim was to explore how patients make decisions around knee replacements, and to understand the factors important in those decisions.

3.3 Methods

This study involved two stages: the first used focus groups to generate a range of patient views; the second used in-depth interviews to explore those views to a depth difficult to achieve with focus groups alone.[79] Focus groups took place with patients who had already had a replacement, and interviews took place with patients who were either waiting for a knee replacement, or considering having one.

3.3.1 Research Team

Dr A. Adams and Dr A Realpe (both part of my supervision team) provided methodological advice, facilitation of focus groups, and independent cross checking of thematic framework. Both have an interest in orthopaedic decision-making, and have been involved in patients' decision-making in orthopaedic trials. Mrs P Scott, a member of the public, facilitated in focus groups, interviews, and analysis of qualitative data. Mrs Scott was identified through University/User Teaching and Research Action Partnership (UNTRAP), a university organisation putting interested members of the public in touch with researchers. Mrs Scott was an active member of the team at each stage of the project, from the generation of the study protocol to the dissemination of findings. Aspects included public information leaflets, recruitment, relevance of the aims and objectives, methodology, and analysis.

3.3.2 Theoretical framework

The concept of different stages to decision-making has been described in the literature previously.[76,77] Elwyn et al. describe the theoretical construct of a deliberation phase and a decision-making (also called a determination) phase.[75] I used Elwyn's theoretical framework to inform the development and analysis of this study. Examining different points along the patient pathway ensured patients representing both the deliberation and decision-making phases were included. The stage of the decision-making process has not been addressed by any previous study.

3.3.3 Interview and focus group conduct

I conducted all focus groups and interviews. Focus groups were facilitated by either Dr Adams or Dr Realpe. Mrs Scott, a patient member with little qualitative experience, was present for both focus groups and four interviews.

Focus groups and interviews took place at the location most convenient for the patients. Sites included University Hospitals of Coventry and Warwickshire (UHCW), the patients home, and by telephone.

3.3.4 Sampling

Purposive sampling across age and gender was conducted to achieve a spread of diversity early in the study. This was essential to avoid unnecessary patient interviews (and therefore patient burden).

The ability to recruit Asian, Black, and Chinese patients was limited because these denominations make only 3-12% of the demographic of the geographic area.[80] Additionally lower rates of utilisation can be expected in these groups.[72] However, every effort was made to include these participants.

Socioeconomic status was monitored using the Index of Multiple Deprivation (IMD 2010) as reported through the national census.[81]

3.3.5 Focus groups

Patients who had a previous total knee replacement for OA at UHCW on or before 30th April 2013 were identified through medical coding. Sequential patients, working backwards from the 30th of April, were send invitation letters for the focus groups. One hundred invitation letters were sent in October 2013 or February 2014 using an "opt in" approach. Focus groups took place in December 2013 and March 2014.

A guide for the focus groups was produced after discussion within the research team to identify key areas that were deemed important (see Appendix I). This was used as a guide only, with the aim of the focus group being the generation of themes. Focus groups lasted approximately two hours with six participants in each group.

3.3.6 In-depth interviews

I analysed the focus groups and produced the interview schedule (see "analysis" below). Dr Adams and Dr Realpe crosschecked both the analysis and schedule. The schedule (see Appendix II) was used as a guide to the range of topics covered in the focus groups.

I targeted two study populations during the interview phase. The first was patients who had decided to have a knee replacement operation (decision-making phase). Patients on the waiting list for a knee replacement and recruited to a multicentre cohort study over a one week period in July (4th to the 11th) 2014 were approached to participate in the interviews. The cohort study was designed to develop a prognostic model for patients considering knee replacement (see Chapters 6 and 7).[82]

The second target population was patients who had been seen in secondary care but had not yet decided to have a knee replacement (deliberation phase). Patients were identified through operative lists for knee arthroscopy with a diagnosis of OA from November 2014 to December 2014. Again, an "opt-in" approach was used with purposive sampling. Although these patients were not actively considering a knee replacement, they had significant OA of the knee such that they were being seen in secondary care. Therefore they were felt to be an appropriate group to target.

3.3.7 Analysis

Thematic analysis was used to analyse the data: this term has been used in many different situations to describe different approaches to qualitative data analysis.[83] For the purposes of this research project, with the authors coming from a predominantly realist perspective, this involved an inductive (bottom up) thematic analysis with a predominantly semantic development of themes.[79,83] This process took place within the bounds of the theoretical framework of deliberation/decision-making previously discussed.

I conducted the analysis with input from Mrs Scott. Mrs Scott has no specific training in the analysis of qualitative data, but her role in providing a member of the public's opinion was invaluable.

Focus groups and interviews were recorded with a digital tape recorded and transcribed and data were organized with the help of computer software.[84] One participant of an interview declined to have the conversation recorded; therefore the interviewer's notes were used for analysis. At the start of focus groups all patients gave their names to aid identification between participants when listening to the recording.

Each member of the team contributed to the development of a coding framework. This coding framework was informed by regular meeting of the research team. The process of searching for themes, reviewing themes, and defining and naming themes was conducted in line with recommendations of Braun and Clarke.[83] Analysis and data collection continued simultaneously. This iterative approach to data collection and analysis allowed the full exploration of emerging themes. Data collection stopped when no new themes were emerging from the data collected. When necessary, transcripts that had already been coded were revisited when a modification of the coding framework and themes took place.

Dr Realpe cross-referenced 10% of the interview data to test the validity and reliability of the coding data. Reliability statistics (percentage agreement and Cohen's Kappa) were calculated by software available online.[85] Instances of one coder using multiple references when the other coder had included one larger reference were resolved by using the main coding topic for each coder and including it as one variable.

Various methods were used to improve trustworthiness. Credibility has been addressed by triangulation of decision-making stage and member checking (member checking refers to participants of the study reviewing both their transcripts and concepts that had been derived from them).[86] Additionally, the research team felt that the participants were very open, especially within the focus groups. Although focus group setting may be considered harder to gain an inclusive and open dialogue due to group dynamics,[79] we found frank and open discourse with an abundance of personal and sensitive information disclosed. This was undoubtedly helped by the involvement of Mrs Scott, a member of the public and advisor on the study. I have provided a thick description of the setting, situation, times, and people to address issues of transferability; however, a caveat exists in that all participants in our study were engaged with secondary care. Dependability is closely tied to credibility, and the use of "overlapping methods" of focus groups and interviews combined with detailed description of the study process has helped to address this.[86]

3.4 Results

3.4.1 Patient numbers and demographics

Six patients took part in two focus groups (12 patients total). This represents a 12% response rate to the "opt in" letters. Demographic details for both groups can be found in Table 5.

Table 5: Demographics of included patients in focus groups

Patient	Gender	Age	Ethnicity	Sociodemographic class (decile)
1	M	72	White British	17882 (5)
2	F	76	White British	20924 (6)
3	M	71	White British	22203 (6)
4	F	68	Indian	21358 (6)
5	F	71	White British	18732 (5)
6	F	67	White British	26766 (8)
7	M	76	White British	12697 (3)
8	M	72	White British	13458 (4)
9	F	57	White British	16472 (5)
10	F	77	White British	182 (1)
11	M	72	White British	22835 (7)
12	F	82	White British	18702 (5)

Using the Index of Multiple Deprivation 2010 ranks for Lower lay Super Output Areas (LSOA) (1=most deprived, 32,482=least deprived). Decile – data ranked from 1 (highest level of deprivation) to 10 (lowest level of deprivation) by dividing into 10 equal groups.

Eleven patients taking part in a cohort study developing an outcome prediction tool for patients considering a knee replacement were approached,[82] with six agreeing to take part (decision-making phase; 55%). Eighteen patients either waiting for or having received a knee arthroscopy were approached for the deliberation phase interviews, with four taking part (20%).

Table 6 demonstrates the demographic breakdown of patients involved in interviews. Only 5% of patients identified for interviews were of Asian origin, which does not reflect the population that UHCW serves (12-13% Asian origin).[80]

Table 6: Demographics of participants in interviews

Patient	Stage of decision-making*	Gender	Age	Ethnicity	Sociodemographic class** (by decile)
1	Post (waiting list)	F	68	White British	31755 (9)
2	Post (waiting list)	M	64	White British	18479 (5)
3	Post (waiting list)	M	68	White British	32096 (9)
4	Post (waiting list)	M	78	White British	30195 (9)
5	Post (waiting list)	F	52	White Other	26469 (8)
6	Post (waiting list)	M	63	White British	24905 (7)
7	Pre	M	73	White British	22006 (7)
8	Pre	F	70	White British	22552 (7)
9	Pre	M	51	Asian	11032 (3)
10	Pre	M	53	White British	2030 (1)

**Stage of decision making refers to deliberation (Pre) or Decision-making (Post). *Using the Index of Multiple Deprivation 2010 ranks for Lower lay Super Output Areas (LSOA) (1=most deprived, 32,482=least deprived).*

3.4.2 Reliability

Percentage agreement of coding into the major themes was 77%, with Cohen's Kappa 0.72. This represents a "satisfactory" level of agreement, using both a liberal and conservative measure of reliability.[85]

3.4.3 Theoretical model

As previously discussed I used a theoretical model of decision-making to inform the study – that of deliberation and decision-making. The original paper by Elwyn et al. does not make clear the boundary between these two stages, although "integrating deliberation inputs" to make a choice is part of this. Within this study, I found a decision-making threshold marked the boundary between these two stages. This threshold, describing the point at which coping with the status quo is no longer acceptable, has been described in the literature previously,[76,77] and was recognised by patients in both the deliberation and decision-making phases. Indeed it was universal in our study:

"It's like little nails going in the coffin…there are lots and lots of different things but they don't go away, they just build up on you. (Interview 6)

"But yes, once I've made the decision and I say, yeah I can't cope, my quality of life is really going down the pan..." (Interview 8)

"No, I think weighing up the pros and cons and if you're in a lot of pain I think you just go for it." (Focus Group 2)

"But still if your pain's bad enough, and you can't get about, you've got to have it done, and that's the top and bottom of it, isn't it?" (Focus Group 1)

Factors that affect the deliberation process alter the point at which the threshold is reached – the so-called "moving target" referred to by Dosanjh.[77] This is key, as it indicates that the boundary between the deliberation and decision making stages is the decision-making threshold. Therefore, for the purposes of this chapter, I will discuss the factors that affect the deliberation process, and therefore the threshold to decision-making. These factors, when causing a negative impact on a patient's life, are like "little nails going into the coffin", bringing the person closer to deciding to have an operation.

Patients that were either at the deliberation or decision-making part of the theoretical model were compared to assess if there were differences in the important factors. No apparent differences were found across the range of themes identified in this study: therefore they are presented combined. Additionally, member checking did not alter the final results of the study.

3.4.4 Factors affecting decision-making

Nine themes emerged from the data that influenced the deliberation process. These were:

- Stress from deliberation
- Expectation of outcome
- Preferred model of care
- Sources of information
- Personal situation
- Mental state
- Coping strategies
- Loss of control
- Trust in doctor

Each theme is explored in turn.

Stress from deliberation

Patients reported that there is a large degree of stress associated with the deliberation process:

" It is stressful actually… It is difficult to make a decision." (Interview 9)

"it is a daunting thought and I can understand why a lot of elderly people that have never had an operation, never been in hospital, how difficult it must be" (Focus Group 2)

"It is an anxious time." (Focus Group 1)

And this stress is something that is constantly there:

"at the moment it's there and it's hanging over you, and you know it's there and it'll kind of rear its little nasty head every now and again as well, because you know it's there," (Interview 8)

However, there is a release of that stress once the decision is made:

"It can take a burden off you." (Interview 7)

"It was a relief that I could see there was a way forward of ending the pain…" (Interview 1)

"Once I've made the decision I will be fine." (Focus Group 1)

"it is like a weight's lifted off your shoulder, I knew that that I needed an operation." (Interview 6)

This idea has wide ranging implications for the decision-making process when considered alongside the decision-making threshold because it would suggest that once that threshold is reached, it is unlikely that patients will move back into the deliberation phase. However, any unwillingness of people to revisit a decision could also represent hindsight bias (i.e. people tend to justify their decisions when they think they made the right choice). Based on these finding is not possible to state which one is dominant, but one interviewee's comments suggested that justification based on thinking she made the correct decision was not present:

"Although you've made a decision there is still a worry in your mind. Not sure if it is a good decision or a bad decision." (Interview 9)

People with depression are more likely to ruminate over decisions than non-depressed people.[87] Therefore, although relevant throughout our sample of patients, this may have a larger effect on patients that have depressive symptoms.

Expectation of Outcome

Expectation of outcome relates to expectations both if treated with a knee replacement and if not treated. Most people considered their knee would get worse if not treated:

“It was a worry if I didn't get it done that it was only going to get worse.” (Interview 4)

“And that is why I thought oh I had better have it done quick I am going to be a cripple type of thing.” (Interview 1)

And they also considered their knee would improve if treated:

“It can't be as bad as the pains you were going through before you had it.” (Focus Group 2)

"I know you would never get back to 100% but I would expect at least an 80% improvement after a knee operation." (Focus Group 1)

However, some participants demonstrated unrealistic expectations:

"I am going to be grand and I can go back and do what I used to do i.e. gardening, golf, (inaudible 00:27:32) running, jogging, walking and everything to a better standard than what I have at the moment." (Interview 10)

Expectations of outcome were therefore fairly consistent in that patients felt they would get worse if not treated, and better if treated. However, differences were based on the *degree* of change in their health status. It is unclear from this study if these expectations can be managed (with a potential effect on post-operative satisfaction).[88]

Sources of information

This theme is intimately linked to expectation of outcome, as it is the information received that shapes expectation. It also forms two parts; the first is the sources of information; the second the amount of information. Patients used a variety of sources of information. All participants had discussed outcome with friends and family, particularly with people who had previously had a knee replacement. A common perception was that this was the most valued source of information:

"I saw the GP, consultant, but the one who knows most is the one who is going through it." (Interview 7) “talking to various people that had had it done, they said ‘oh you ought to have it done’ old rugby mates of mine who had had hip replacements and knees and everything else, they reckoned it worked very well.” (Interview 2)

“You learn a lot more in the waiting room, because they have all gone through different procedures on their bodies. A doctor can go through what they can do for you and you can go through that procedure but then you hear more in the waiting room because they have had it done.” (Interview 7)

“You can see things on the Internet and read things but when you actually speak to somebody who’s done it and she’s got no reason to lie. She’s not trying to promote it for any reason.” (Interview 10)

“I did it for reassurance, hoping that they would say yes, it was a great success, and I feel fantastic.” (Focus Group 1)

These last two quotes are particularly interesting, as it suggests some people are only looking for reassurance, not new information. It also suggests a level of distrust of the medical profession, potentially “trying to promote” an operation. This is intimately linked to the theme “Trust in doctor”. However, the preference for information from friends and family, although prevalent, was by no means ubiquitous.

“I would just speak to the surgeon.” (Interview 8)

“Being able to talk to your surgeon… can give you an idea of what you should expect.” (Interview 8)

“Yeah I looked it up on the Internet and things like that… I even watched the operation.” (Interview 3)

However, some people preferred not to use the Internet and medical professionals:

"I just wouldn't bother actually because it wouldn't even pass my mind to look for any medical advice or anything on the Internet." (Interview 10)

"I don't really talk very much to the GP…" (Interview 1)

Additionally, people wanted to know different amounts of information:[22,47-49]

"I didn't want any pre-information because I was too squeamish." (Focus group 1)

"But if I had anything, even if it was the worst scenario, I'd rather know, I'm better if I know about things and read about it. Not that I look and read and think, oh, I've got that, that and that, but I am better for, you know, sort of knowing about things." (Focus Group 1)

Differing preferences for information is a finding consistent with reports in the literature regarding other healthcare decisions.[47,48] Interestingly, attempts at trying to predict the amount of information patients may want have been unsuccessful.[49]

Personal situation

Someone's personal situation is individual to him or her but can have a large effect on the deliberation phase. Subthemes identified included: motivation (for a specific task, e.g. walking further), or a more generalised return to a "normal life":

"one of the factors I've considered is that I am now, I am proud to say, a grandfather…" (Interview 6)

"I've got two children abroad at the minute and I need to be able to get there and have a bit of time, basically." (Interview 4)

and work and financial concerns:

"Because I have cut my hours down and it affects my wages as well." (Interview 7)

"I'm self-employed and the biggest thing is I've got to be able to work." (Interview 4)

Two further subthemes deserve special mention. Firstly social pressure was felt to occur, especially from loved ones. This is intimately linked to feelings of inadequacy or of letting people down:

"I said to them, "My husband will go with you, you go and I'll stay at home." So they said, "No, we don't want to go without you," so then of course I felt bad that I'd let them down and you're not doing things you would normally do with your friends." (Interview 5)

"R: No, just pressure from –
I: Pressure?
R: - well let's just say loved ones (laughter)." (Interview 5)

Secondly, personal commitments occasionally had an overpowering effect on the process:

"I: Did you worry about having your knees done, because of your home environment?
R: It wasn't worrying for me having my knee done, it was worrying about...
Your son? (Focus group participant asking the question).
R: My son." (Focus Group 1)

Mental state

Broadly speaking, this theme can be divided into the psychological consequences of having knee OA, and the psychological aspects of considering a knee replacement. People experienced anxiety, depression, lack of pleasure, feelings of dread, feelings of inadequacy, social withdrawal, and frustration when suffering from knee OA.

"I had about 48 hours that I ... well I didn't answer the phone for starters. I didn't go out apart from walking the dog." (Interview 8)

"I would say, yes, I've had anxiety, I've had depression." (Focus Group 2)

"My knee was so painful and jarring and I had that horrible feeling inside where every step you make is it going to be a jarring pain." (Interview 3)

"when it's just my husband and I alone at home, I have cried every now and then." (Interview 1)

However, some people displayed determination to continue, despite the psychological pressure:

"I wouldn't give into it until I absolutely had to give into it." (Interview 8)

"Okay, fine, so live with it, which I did." (Interview 1)

When considering treatment options fear was the main theme that emerged – there were a range of fears from damaging the knee further from not getting treatment, through visiting the doctor, fears over the procedure and anaesthetic, and fears over the recovery period and outcome.

"It was a worry if I didn't get it done that it was only going to get worse." (Interview 2)

"I went for my pre-op, and I was really, really scared, and I just said to this woman who was sitting next to me waiting, I said, "Are you scared?" and she said, "Bloody hell, but I've got to get on with it, haven't I? You either want it or you don't." (Focus Group 1)

"Oh yes. I think being knocked out is the worry." (Interview 9)

"What worries me about a knee replacement right, how long does it last?" (Interview 7)

Coping strategies

Coping strategies affected the ability of people to cope with their symptoms, feeding into the deliberation process and the decision-making threshold. They can be divided into physical and mental. Physical coping strategies included altering the work/home environment, altering the way things are done, avoidance of activities, getting help from others and keeping moving.

"My office is two floors up so I have to do the stairs…they brought my laptop down and said work from down here." (Interview 5)

"I tend to try and walk as much as I can to ease the problem which I find helps." (Interview 10)

"So I haven't played golf for over 18 months now because of the fear of aggravating the problem." (Interview 10)

Mental coping strategies were more varied. However, a remarkably common theme emerged of stoicism and a positive mental attitude.

"It's not too bad, I put up with it." (Interview 2)

“But no, people give in, they give in to things and if I can’t change it I don’t worry about. There’s no point.” (Interview 8)

When considered in light of the decision-making threshold, it appears that people cope using both the physical and mental coping strategies above; however, they reach a point in their personal lives and symptoms where their coping strategies are no longer able to effectively manage.

Loss of control

Loss of control can again be divided into physical and mental. Physical loss of control occurred due to knee problems in everyday life, and affected deliberation directly:

“One particular day I got halfway round and I just couldn’t walk and I hadn’t had that before. I felt quite scary about that, that you know it should come on so quickly.” (Interview 1)

“Because I couldn’t suddenly nip out, well normally if you are nipping across the road, but when you’ve got bad knees, an unpredictable result you can’t do that sort of thing.” (Interview 6)

Mental loss of control was associated with having an operation. There were feelings of vulnerability and reliance on others associated with this, which affected the deliberation process:

“Well you do lose control because you’re putting your hands ... you’re putting your body, your knees, in the hands of another person and you don’t have any control over that at all. You give them your control over your knees.” (Interview 8)

Additionally, it was clear that the pathway of care could make this feeling worse:

"When I had my second one done I was booked in, I came here 7 o'clock in the morning, ten to 12 I was sent back home. I was sent for again, arrived here at 7 o'clock, 1 o'clock I was sent back home. I came in the second time, the third time and I sat until 1 o'clock and I thought, "Am I going to do that journey to the theatre, or am I going to phone my husband to come and collect me?" but I went to the theatre." (Focus Group 2)

Or it could improve the feeling:

"You were given the choice of where you had it, so that helped me." (Focus Group 2)

Closely related to the idea that loss of control and the subsequent feelings of vulnerability could be improved by the process of care is the trust that the patient had in the doctor, which is described in the next section.

Trust in doctor

A person's trust in their doctor appeared to affect many other themes within their deliberation process. It affected peoples' mental state positively:

"I knew that I needed somebody that was really going to do the best for me and I felt that he was going to do that. So I walked out of there in a far better frame of mind than I'd actually walked in," (Interview 8)

"Oh yes you have got to have confidence and trust otherwise you wouldn't do anything for anybody." (Interview 5)

and negatively:

"But he didn't inspire me with a lot of confidence…I thought well for the sake of five minutes it was hardly worth it really." (Interview 9)

An aspect of trust in the doctor was based on the process of care. As discussed previously the process of care can harm the relationship between doctor and patient:

"Dr [T] said, "I will be doing your operation" ... And I felt at ease with him because quite frankly he went through the procedure, what would be happening, where you would be going. And I thought I feel at ease now, I feel good. And when I saw another doctor this morning and I thought I have never seen him before." (Interview 10)

Another key factor in the establishment of that relationship was the patient's preferred consultation style, and the style that they actually received. Originally this concept of "Preferred medical model" was coded together with "Trust in doctor"; however, during the process of reviewing themes they were included in the final model as two distinct themes.

Preferred medical model

There was a clear dichotomy of experiences and views of patients as to which model of care they had experienced and preferred. Some patients had experienced informed or shared decision-making interactions, where they were asked to make the decision. This lead to a variety of reactions, including it being received well and the belief that it was the appropriate way to conduct the interaction:

"I don't think anybody can actually tell you, they can advise you to do it, but at the end of the day it's up to you." (Focus Group 2)

“I think it is going to be more or less 50/50. I think he is advising you for the best thing and you are going to turn around and say ‘well I don’t feel as though I want to do it or not’.” (Focus Group 1)

However, this model also led to anxiety. This next quote is particularly relevant, as the lady had already had one knee operated on, and was on the waiting list for the next. She described the consultation for her first operation as paternalistic (which she thought of as a “relief”), and the second as being given the options and asked to choose (informed decision-making):

“I was just thinking well hang on a second you know and I was almost not believing myself in it actually needing doing… I was feeling that I wasn’t ... I didn’t have the right criteria or enough of the right criteria to actually have a knee op. That was the thing. Then it started making me think well maybe I’m not.” (Interview 1)

She was so concerned about the indication for her second operation she wanted reassurance from the interviewers that it was indicated – this was three months after the consultation, and demonstrates the level of anxiety that can be provoked by this model.

Also, asking the patient to decide can be seen as an avoidance of responsibility:

“Yes, because I think if they’re going to throw a load of options at you and then they’re throwing the ball back in your court, haven’t they, and you make the decision, how do you want us to do it?” (Interview 6)

The picture for paternalistic care was also mixed, although the volume of responses that described paternalistic care being well received far outweighed the number of responses supporting shared or informed decision-making (29 and 9 respectively).

“R: His comment was, “Yes it needs doing.” So I go along with it.

I: How did you feel about that?

R: I thought yes thank God for that.” (Interview 4)

However, it is not clear if this is because people have made their decision before meeting the orthopaedic surgeon (they have reached their threshold of coping) and therefore are happy with this process when it occurs: one comment demonstrates that this has a part to play:

“You’d have to have more information to be able to talk to your consultant and convince him that your operation is totally necessary.” (Focus Group 2)

Despite this ambiguity, it is clear that in these patients a paternalistic interaction leads to a relief (perhaps related to trust in the doctor, the stress from deliberation, and the decision-making threshold), and increased confidence. Supporting this was the belief that the doctor, due to his or her expertise, should be the one to decide:

“You as an individual might make the wrong one whereas he is the professional and he knows best with the problem that I have got.” (Interview 10)

“It was a relief that I could see there was a way forward of ending the pain and also that he was so confident that that’s what needed to be done.” (Interview 1)

This contrasts quite starkly with the pre-operative information theme, where information from friends and family was generally considered of more merit. This demarcates two important issues between these themes – the patients' desire and actions to receive information, and the patients desire to be involved in the decision-making process. Although it could be expected that both would co-exist, that is not the case within our sample. This finding is consistent with other literature on information about a decision, and the decision-making process itself.[47,48]

However, there were instances of the paternalistic model not being well received, again consistent with the finding of different patients preferring different styles.[48]:

"Right, so you don't even get to the decision-making process, it's not up to you, it's somebody else." (Focus Group 2)

Previous studies have demonstrated that younger patients have more desire to be involved in medical decision, but our data did not support this.[47] This could be due to a small sample size.

Overall we saw a preference for the paternalistic model of health care, however there were contrasting beliefs of what approach was best, and of how best to approach decision-making.

3.4.5 Proposed model of decision-making

The universal finding of the "decision-making threshold", combined with the stress that the deliberation process places on an individual, led to the development of a model of decision-making (Figure 4). Central to this model is the idea that once a person has passed the decision-making threshold and made their decision they are not likely to pass back into a deliberation phase. This is likely to act in concert with the hindsight bias, and the magnitude of each effect is not clear from this work; however, the implications for the provision of information and the management of expectations are significant.

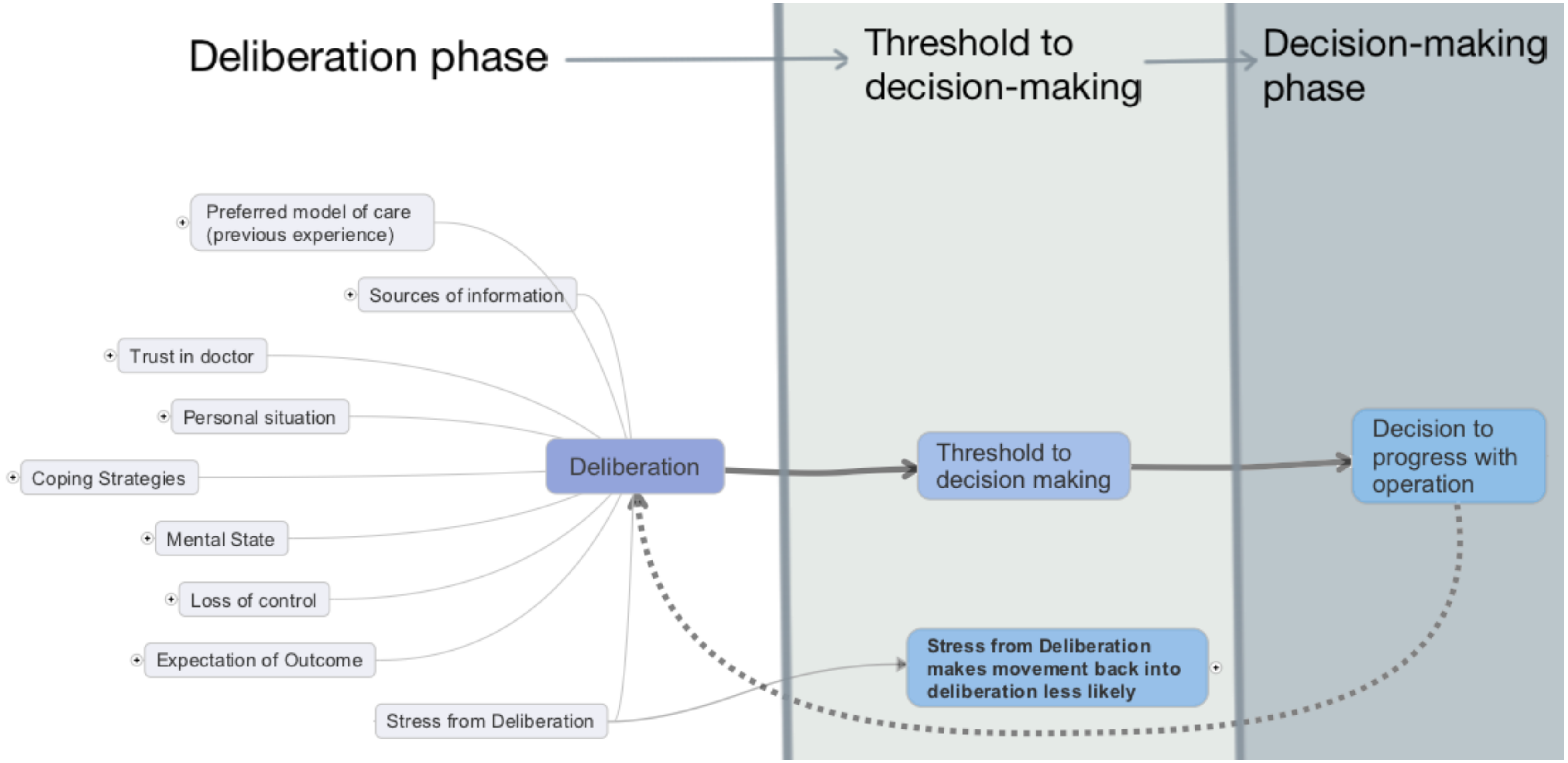


Figure 4: Decision-making model

3.5 Discussion

This study has demonstrated that during the deliberation phase of decision-making for knee replacements nine key factors play into the decision-making process: stress of deliberation, expectation of outcome, sources of information, personal situation, mental state, coping strategies, loss of control, trust in doctor, and preferred model of care. This then leads to the decision phase. The decision-making threshold marks the boundary between deliberation and decision. Interestingly, the factors that play into decision-making are consistent across decision-making stages.

The strengths of this study include: its focus on one area of decision-making, namely preference based decision-making in total knee replacement; the inclusion of people at various stages of the decision-making process; the broad based research team, including a member of the public who was involved at all stages; the inclusion of a range of ages, genders, and ethnicities within the study; the comprehensive analysis; and thoughtful efforts to demonstrate the trustworthiness of the study.

Weaknesses of this study include it being run over two sites. Although these sites cover a population with a wide rage of sociodemographic characteristics, the range of ethnicities that were present within the study population was limited. This likely reflects to some degree the population the study was based in, but also reflects utilisation rates of orthopaedic services. Medical coding data was used to identify some patients and this demonstrated the proportions of ethnicities were not reflective of the population as a whole. Utilisation of healthcare has been found in previous studies to alter by race.[37,38] To counteract this, the research team went to extensive lengths to ensure as much diversity as it could, and the study population roughly reflects the population demographics of the patients presenting to secondary care with knee OA. However, it is likely that the ethnic minority participants in the study are systematically different to those that underutilise healthcare. Compounding this is that the use of an "opt in" procedure to recruit participants inevitably leads to selection bias.

I have compared answers from patients across different methods of data collection (focus groups and interviews). This may result in differences being apparent due to the collection method, for example people in the focus groups not feeling able to speak up, or providing a more ubiquitous point of view.[79] Given the diversity of opinion and the personal nature of some of the information disclosed in the focus groups I do not think this was a particular issue. However, some differences may persist. Additionally, different methods were used in conducting the interviews, including being conducted on the telephone, in the patient's home, or at UHCW. This could have altered the discourse, but we felt this was unlikely and, by making entry into the study more convenient, will have addressed some aspects of selection bias.

Reliability statistics for the coding framework were satisfactory. I am confident higher reliability statistics would have been achieved if not for an oddity in the coding framework that allowed the same reference to be coded in two different places (i.e. "motivation" and "mental state"). Altering this would have improved the apparent reliability of the coding. However, I felt they were important concepts to separate, and did not feel it altered the conclusions of the work. This example highlights the complex interplay of all nine factors across the deliberation phase, and acts as a caveat for considering any one in isolation.

A further weakness is the power differential generated by the interviewer being an orthopaedic surgeon in training. This may have resulted in more guarded responses. However, this effect may have been reduced by the presence of a member of the public for most interactions.[46]

The themes identified in this study are consistent with themes identified in other studies across a range of ethnicities, countries, settings, and decision-making stages.[67-69] In contrast to other investigations, this study is the first to include patients at all stages of the decision-making process, which has allowed the triangulation of our results, and a more reliable account of the deliberation process. This has particular relevance when considering the threshold to decision-making, as I was able to examine it from both sides of the equation. Additionally, only two other studies have examined decision-making in the U.K., both using a population consisting solely of knee replacement patients.[71,72] These studies included only patients on the waiting list (i.e. past the deliberation phase) and are therefore subject to limitations of retrospective studies. This study confirms their findings, but also improves their trustworthiness and transferability by including a wider population base.

Only three studies have included only knee replacement patients in the deliberation phase.[67-69] All these studies took place in the USA. One study only interviewed Black Americans, and therefore has limited transferability.[67] Another only focused on the concerns of patients, and not the wider decision-making process.[69] The third used focus groups to discuss decision-making with patients who had a diagnosis of OA knee in primary care.[68] This study demonstrated similar themes but the use of focus groups, which may not gain sufficient depth of understanding of issues, combined with the use of a single outpatient institution and a small sample size encourage the authors to warn that "It is not possible to assume that the decision-making factors identified by the patients in this study can be generalized to the population of patients with OA who are considering TKA [Total Knee Arthroplasty] at large." [68]

Previous literature has described a threshold to decision-making in investigations into decision-making in knee and hip replacements[76]and in hip replacements.[77] I have taken this work further, by demonstrating this threshold as the boundary between deliberation and decision-making, and establishing that there is a different level of stress at these different stages. This had particular relevance when considering the inclusion of participants at different stages of the decision-making process within this study. All participants in our study demonstrated a threshold to decision-making. This is the first study that has demonstrated this finding in patients' at different stages of the decision-making process in knee replacements. Understanding this threshold, and the nine factors that influence it, has implications not only in routine clinical practice to facilitate patient-centred care, but also in the development of interventions aimed at supporting decision-making, or facilitating information giving. When combined with the finding that the deliberation process was stressful (a universal finding in our study across all stages of decision-making), these finding suggest that patients are less likely to move back (from decision-making to deliberation) once the threshold has been reached (and they have moved from deliberation to decision-making). This relationship has been demonstrated in Figure 4.

Furthermore, the model of care that patients wanted varied, although there was a preference for a paternalistic interaction among those in our study. This is an interesting finding as it is contrary to current political movements within the NHS.[46] Given the sample size, I would recommend further validation of this finding in different populations, and investigation into other pathologies and interventions.

One of the over arching findings from his study was the complex interplay between all of the themes. It appears that all the factors identified work together to shape a person's decision, with different factors having different importance to different people. There was one instance of a patient with one overriding theme, which dominated all others (her personal situation dominating her thoughts on a knee replacement due to caring commitments). However, this patient finally decided to have a knee replacement, again using a complex interplay of factors.

3.6 Conclusion

The themes identified here interacted comprehensively with one and other, the result being a complex interplay of factors that affect the deliberation process, the threshold to decision-making, and the ultimate decision. An awareness of the deliberation phase, the factors that influence it, the stress associated with it, preferred models of care, and the influence of the decision-making threshold will aid useful communication between doctors and patients.

Future work, examining how this information might be best translated and utilised in the clinical environment is an exciting avenue. This is one of the key elements in addressing the three crucial areas set out in the introduction; differences in utilisation rates,[31] a high dissatisfaction rate,[25] and increasing demands with financial constraints.[27] One aspect of this is understanding how outcome prediction would affect the decision-making process for patients, what information they would like, and when in the pathway it would be of most use. The next chapter deals with these questions.

Chapter 4. How outcome prediction could affect patient decision-making in knee replacements: a qualitative study.

This chapter uses focus groups and interviews to examine what sort of information patients would want from an outcome prediction tool, how it could affect their decision-making process, and at what part of the pathway such a tool should be used. The results demonstrate that an outcome prediction tool would have most effect targeted towards people at the start of their treatment pathway, with a "bottom line" prediction of outcome. However, any effect of a poor outcome prediction on expectation and decision-making is likely to be blunted by the optimism bias.

4.1 Declarations

Aspects of this chapter have been submitted for publication:

T. Barlow, P. Scott, D. Griffin, A. Realpe. How outcome prediction could affect patient decision-making in knee replacements: a qualitative study. Submitted to BMC Musculoskeletal disorders February 2016

Aspects of this chapter have been presented at an international conference:

T. Barlow, P. Scott, D. Griffin, A. Realpe. How does outcome prediction in knee replacements affect patient decision-making? 23rd annual meeting of the European Orthopaedic Research Society.

This study was approved by the Dyfed Powys Research Ethics Committee (13/WA/0140).

Dr A. Realpe provided independent cross checking of thematic framework. Mrs P Scott facilitated in focus groups, interviews, and analysis of qualitative data. An external company conducted transcription of focus groups and interviews.

4.2 Introduction

Many previous studies have attempted to identify predictors of outcome, examining various factors including surgical factors and patient factors.[22,89-94] These studies will be discussed in detail in the next chapter; however, to date, none have been successful in developing a tool that can usefully predict outcome. There are currently several investigations into the development of such a tool,[22,95] including the investigation towards developing a prognostic model described in chapters 5 and 6.[82]

Alongside this quantitative research, research into understanding what factors are important in patients' decision-making has gained momentum. Multiple studies across multiple countries have demonstrated a remarkable consistency in important factors that influence patients' decision-making, as discussed in chapter 2 and 3. A key concept, and relevant to outcome prediction, is that of the deliberation/decision-making model proposed by Elwyn.[75] This splits decision-making into a deliberation phase, and a decision-making phase. Additional studies have demonstrated a "decision-making threshold" – a moving target of the point at which a patient changes from deliberating the decision to making the decision, usually the point at which coping with the status quo is no longer acceptable.[76,77] The previous chapter reported the findings from a qualitative study, where a novel decision-making model was presented that is consistent with these previous studies.

However, what is unclear, and has never been studied before, is how an outcome prediction tool would affect patients' decision-making. Therefore our aim was to explore how a (fictitious) outcome prediction tool could affect patients' decision-making.

4.3 Methods

This study occurred in parallel with the investigation into patient decision-making presented in chapter 3, using the same research team (with identical contributions). Two stages were performed: the first used focus groups to generate a range of patient views; the second used in-depth interviews to explore those views to a depth difficult to achieve with focus groups alone.[79] Focus groups took place with patients who had already had a knee replacement, and interviews took place with patients who were either waiting for a knee replacement, or considering having one. Examining these three points in the patient pathway allowed us to include the two stages of the decision-making process proposed by Elwyn, namely deliberation and decision-making.[75]

4.3.1 Conduct of focus groups/interviews

The usefulness of information an outcome prediction tool may be able to provide was tested with all participants via the use of a fictitious report containing information that an outcome prediction tool may contain. There were multiple versions of this report, which evolved based on patient feedback and used different styles of presentation. These reports varied from "bad" to "good" outcomes, with improvements ranging from 5-20 on the Oxford Knee Score. Key aspects included a summary of predicted pain post-operatively and a summary of predicted function post-operatively. Text and graphics were used, with comprehension and preferences noted. An extract from this report is on the following pages, with an example of a full report available in Appendix III.

The bottom line

One year after the operation:

There is a 30% chance you would not have had the operation if you could go back in time.
This means that if 100 people in your position had a knee replacement, 30 would not have the operation if they could go back in time

There is a 20% chance you would not recommend a knee replacement to a friend of member of your family.
This means that if 100 people in your position had a knee replacement, 20 would not recommend the treatment to a friend or member of their family.

There is a 15% chance you will still have pain in your knee after the operation.
This means that if 100 people in your position had a knee replacement, 15 would still have pain after the operation.

Your knee will work better after a knee replacement – this improvement is likely to be below average.
This means that most people in your position would improve more than you would. However, a small improvement may be very worthwhile to some patients, whereas a large improvement may not be worthwhile to another. It is up to you as an individual (with help from your surgeon) to decide if the operation is worthwhile.

Knee outcome report – Pain

Knee pain

Some patients have pain in their knee after they have had a knee replacement.

It is important to note that some patients may have a low chance of having pain and still develop it, and some patients may have a high chance and not develop pain.

Your chance of developing mild pain is 10%

This means that if 100 people in your category received a knee replacement, 10 would develop mild pain.

Your chance of developing moderate to severe pain is 5%

This means that is 100 people in your category received a knee replacement, 5 would develop moderate to severe pain.

THESE CHANCES ARE DEMONSTRATED IN THE DIAGRAM BELOW

Patient without significant pain after knee replacement

Patient with mild pain after knee replacement

Patient with moderate to severe pain after knee replacement

Knee outcome report – Function

How your knee works (e.g. climbing stairs) ***before*** a knee replacement varies from person to person. Therefore, to get an idea of how much your knee may improve, you need to be able to know what it is like before an operation.

We have assed how your knee is works ***currently*** (before your knee replacement) using a scoring system. This is reported on a scale running from 1 (very poor function), to 100 (very good function). Your score is:

50

We expect your score (and therefore how well your knee works) to improve after a knee replacement. Some patients improve more than others.

Some patients find a small improvement in their score results in a **significant improvement in their quality of life. It is difficult to predict exactly how a knee replacement will affect you personally.**

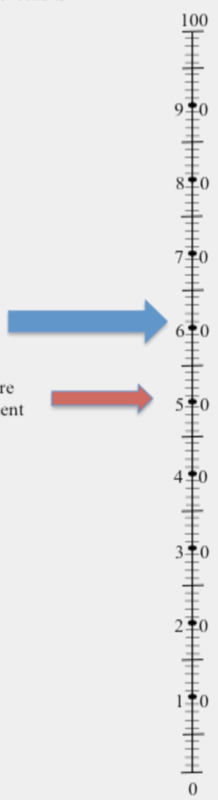
We expect your score to improve by:

10 POINTS

What this means to you is explained in the following pages.

We expect your knee function to improve by about 10 points. This is below average for a knee replacement.

A small improvement in knee function may be very worthwhile for one patient, but not for another. A small improvement on the scale can result in a large improvement in quality of life.



It is important to note that an improvement from 40 to 50 is not the same as an improvement from 50 to 60 – what is important is where you are starting from, and where you end up. This is explained in the following pages.

How the tool could affect the decision-making process overall, and its effect on factors involved in decision-making, was explored. Specific questions, based around topics the research team thought would be important, were asked, but participants were encouraged to provide their own views and options. Pre-defined areas thought critical to cover included perceived benefits of the tool, perceived sensitivities, preference of delivery of tool, its effect on decision-making, and patients' acceptability of being offered alternative treatment on the basis of their personal prediction. Patients' views of alternative treatment was considered relevant as psychological factors appear to account for a large amount of the variability in outcome and, based on current evidence, would be a potential target for modifying risk factors.[89]

4.3.2 Analysis

Analysis was identical to that conducted in chapter 3.

4.4 Results

This study used an identical study population as that described in chapter 3.

4.4.1 Thematic analysis

I identified six major themes within our study. Five of these themes were those identified as potentially important before the study began (perceived benefits of the tool, perceived sensitivities, preference of delivery of tool, its effect on decision-making, and patients acceptability of being offered alternative treatment on the basis of their personal prediction) and one was additional (optimism bias).

Benefits of outcome prediction

Participants were universally positive about the principle behind the tool, feeling that having such information would be helpful:

"If they said that you were going to be pain-free but your functionality wasn't going to be as good, you may not be able to bend it and you would have to walk with a stick. Or if they said the opposite, you're still going to have some pain but your functionality is going to be a lot better then you've got some information to make a decision." (Focus Group 2)

"Yes, because it's giving you a real expectation of what to expect, because basically at the moment all I've got is what happened to my friend" (Interview 1)

There was also the belief that having information in a written format that could be taken away was a worthwhile aim, especially for people who are socially isolated and may not have the contacts with friends or family to discuss outcome:

"It would certainly fill that gap. I mean the fact that we've got lots of family here and down in the South lots of other Africans, it's not really a factor but just thinking of that sort of, there are lots of other people that have come to live here from other countries that don't have a support group, I think that would be really beneficial." (Interview 1)

The type of information the tool conveyed also had positive effects. This was true for predictions that were on the whole positive, where respondents felt it gave them confidence to proceed:

"I think that having made the decision myself before the surgeon said I want you to, that would have confirmed yes, this is definitely the right thing to do." (Interview 1)

"Yes I, I, yes. I'd feel great.

I: You'd feel great.

R: Yes.

I: It'd give you a bit more confidence in going ahead?

R: Yes give me confidence, yes." (Interview 5)

Interestingly, and quite unexpected, were the positive aspects of providing a report that was predominantly negative:

"And he kept saying, "I can't believe how bad you are." And I said, "Neither can I." So, I would have probably thought, "Okay, I'm going to be in the 20%;" **I probably wouldn't have been quite as hard on myself,** because I kept thinking, "Well, what's gone wrong?"" (Focus Group 2)

"But no, it would put things more in perspective I think and then also when you've had the operation if it is not as good as you were hoping it, but you've already been told it might not be, then you've come to terms with that." (Interview 8)

A further aspect of report was that people felt it would likely affect the sources of information that they went to, but they would not use it as a sole source:

"If I had got that before…because I'd done all that before I came to the knee clinic, and for my pre-op, so I still would have asked my friend, but I think I wouldn't have bothered looking on Google at the different things." (Interview 1)

Sensitivities related to tool

Sensitivities related to outcome prediction were also explored. When provided with a poor report some respondents felt that it was a "surprise" and that such information could "frighten people away":

"it isn't what I would have understood heard or expected." (Interview 3)

"don't know about that, I don't know, I think you have got to be very careful that you don't frighten people away from what needs to be done." (Interview 6)

One focus of enquiry, that was identified before the study began by the research team, were that of a poor prediction of outcome being related by the patients to a diagnosis of an "unhealthy psychology". This was based on the fact that psychological factors are likely to be the biggest predictor of outcome.[89] All participants were asked to give their thoughts on this, particularly relevant for the first six participants in interviews, who had completed the baseline assessment for the development of the prognostic model described in chapters 6 and 7. No participant displayed any concerns regarding a poor prediction being associated with an "unhealthy psychology":

"No I don't think it would do anything with mental health, no." (Interview 2)

"It probably wouldn't enter my thinking, no" (Interview 4)

The second focus of enquiry that was identified before the study began was that of patients being aware that a prediction was not a guarantee of outcome. All study participants appreciated this:

"No, it's not. The way you've explained it in there as well, then you're not guaranteeing it, it should be. You're not guaranteeing it." (Interview 8)

"You can't say okay you've got 50 now, I guarantee you'll have 60. This is what you ... I think you should have, but you can't guarantee it." (Interview 7)

However, some participants expressed concern that not all people would see it the way they did:

"you're going to get some comeback ... he's gone the opposite way round, and you've predicted this, that's where you're going to get your comeback. Because they're not going to be happy with what you predicted." (Interview 4)

A further concern of patients was the use of this information to rationalize or prioritise patients for theatre. Some people thought that this was a reasonable course of action, assuming that "the 20%" who have a poorer outcome should be prioritised:

"But presumably these lists are prioritised using a whole variety of criteria and this is just adding to this criteria, surely. They would still have to be prioritised; the most urgent get done first." (Focus Group 2)

However, others were very concerned that this sort of information should not be used for either rationing or prioritisation, and should only be used to provide information to patients:

"R: Well it's a process for the patient, it's not a process for the surgeon…"

"I: It would predict what your eventual outcome would be. And should the surgeon use that when rationalising whether you should have a knee replacement or not?

R: The answer in my opinion is 'no'." (Focus Group 2)

Preferred delivery of tool

There are differences in the amount of information that different patients want in a wide range of medical situations.[47-49] When it came to the outcome prediction tool there was a general preference for a "bottom line" approach and visual displays:

"That would have been brilliant ... I like the picture that says in all probability you may expect an improvement of X per cent, I think that's the way I would like to receive the information." (Focus Group 1)

"I think the fact that it's a visual aid is helpful. I think again, rather than simply having script, to have a visual aid is almost essential. I know I can do that. You can see it physically." (Focus Group 2)

"One has to remember that you are, I mean the people who are having knee replacements might not be mathematicians so might not understand –

I: Yes, absolutely.

R: I think that is good. [Referring to diagram of % of pain]" (Interview 6)

There was a feeling that people would need someone to go through this information with them in a face-to-face context:

"My instinct says it's better to have somebody to go through it with you. I think just receiving it … I found not the easiest thing I've done in the last seven days ... There are some people who can't speak English or understand, they have to be explained and all that." (Focus Group 1)

Trust in the output from the tool was also seen as essential:

"I think you'd need to know where the figures are coming from … one knows that these are just the opinions or whether they are from a clinical analysis or something, you know" (Interview 6)

Two of these quotes reveal information that is particularly relevant to the development of a prognostic algorithm. Firstly, one of the patients thought of the functional gain in terms of "per cent" (when discussing functional gain). This suggests a linear scale, which the Oxford Knee Score is not. This was despite information (both written and verbal) to the contrary. This has implications for how information is displayed, and the understanding that can be expected from patients with non-linear scales. Secondly, trust in the figures was seen as essential, which means that any estimate will have to be precise.

The tool's effect on decision-making

The tool's effect on decision-making was tested on three different groups of people, each at a different stage of the decision-making process: those in the deliberation phase; those just after making a decision, but still waiting for the operation; and those who had already had the operation. The effect of the tool was examined in each group.

Patients who had already had an operation

In this group patients were asked how the tool would have affected their deliberation process, and therefore the difficulties inherent with any retrospective inquiry were present. However, all patients thought that the information would have had the ability to change their expectations:

"R: No, I think weighing up the pros and cons and if you're in a lot of pain I think you just go for it.
R: You'd lower your expectations wouldn't you? (Another member of focus group asking question)" (Focus Group 2)

"it would surely give you confidence if you did the questionnaire and came out into a good category" (Focus group 2)

It was challenging to get this group of patients to distinguish between altering their decisions, and altering their expectations. Interestingly some patients felt strongly it would have had no effect on their expectations if the predicted outcome was poor, but would have improved confidence if the predicted outcome was good. This will be discussed in more detail under "optimism bias".

There was a predominant feeling that the tool would not have affected the decision:

"No, likewise, the same as well, it wouldn't have made any difference because I was in pain and it needed to be done." (Focus Group 1)

However, some people (in the minority) thought that it would have:

“I: do you think [an outcome prediction tool] would have helped?

R: Possibly; it would have been a lot easier.” (Focus Group 2)

“It would probably have made me think deeper about it.” (Focus Group 10

Patients who were on the waiting list for a knee replacement

This group of patients universally would have changed their expectations; however, again there was a division on if it would have affected the deliberation phase, with some patients stating it would have:

“I think I certainly would have thought instead of that initial response when he told me I needed to have it, I might have said I need to think about it a little bit first,” (Interview 1)

And others stating it would not; however, this was less strongly held than the post-operative group, often with a qualifier:

“it would have been nice to know but in, in my situation no it wouldn’t have [altered my decision].” (Interview 5)

Patients who were contemplating a knee replacement

In this group all patients felt that the information in the outcome prediction tool would have affected their expectation and their deliberation. This was a strongly held belief:

"This sort of information are enough to change anybody’s mind" (Interview 10)

"Yes, of course it affects expectations" (Interview 10)

"Yes I think it would be helpful if people knew what their chances were after an operation. I think it would help them make the decision whether to go ahead or not" (Interview 9)

Overall there was a stark difference in how the tool affects decision-making. This result is not unexpected. The deliberation phase of decision-making is stressful, and there is a relief once a decision is made (Chapter 3). Therefore, any new information that comes to light once the decision is made is less likely to change that person's mind. The stress from the deliberation phase appears to act as a barrier to revisiting an already made decision. This is critical when considering at what point in the pathway of care an outcome prediction tool should be used.

When patients were asked directly when they thought this information should be given there was a complete range of responses:

"I think I would like the GP to action this and get it through." (Focus Group 1)

"Pre-op assessment." (Focus Group 1)

"I think the consultant or the consultant's team is or are the best people." (Focus Group 2)

Acceptability of alternative treatment

Alternative treatment (e.g. Cognitive Behavioural Therapy (CBT)) has the potential to improve the outcome from knee replacements. CBT can alter psychological processes, such as coping strategies. These factors could affect outcome in knee replacement and by modifying them before knee replacements outcome could be improved. This (highly theoretical) option was posed to patients by asking if they would be willing to delay their operation to undergo CBT if it would be likely to improve their outcome. A remarkable division between pre and post-operative patients resulted, with post-operative patients universally disagreeing with any delay:

"I don't want to suffer another three months. Go for it, I think." (Focus Group 1)

And pre-operative patients having mixed views:

"Well I suppose I would then if you felt that I ... that's what I needed…Yes. I mean you have to listen to the medical staff, they do ... you know to some degree know a bit better than you do." (Interview 3)

"I wouldn't have wanted it to be delayed." (Interview 1)

Participants were generally not particularly receptive to psychological therapies, which is consistent with the participants' view that a poor prediction of outcome was not associated with an "unhealthy psychology". Interestingly, the protocol for a feasibility trial comparing pre-operative CBT against normal care has been published recently (the HAPPiKNEES study).[96] On the basis of the findings here, recruitment may be problematic.

Optimism bias

Sharot defines the optimism bias as the propensity to:

"Overestimate the likelihood of positive events, and underestimate the likelihood of negative events. For example, we underrate our chances of getting divorced, being in a car accident, or suffering from cancer. We also expect to live longer than objective measures would warrant, overestimate our success in the job market, and believe that our children will be especially talented. This phenomenon is known as the optimism bias, and it is one of the most consistent, prevalent, and robust biases documented in psychology and behavioural economics."[97]

This bias was displayed when examining the effect of the outcome prediction tool. I found that patients who have already had a knee replacement were unwilling to move their expectations down with a poor prediction, but willing to have a good prediction inspire confidence. The optimism bias was displayed across all three groups:

"No because I know within myself you know I'm a pretty healthy guy and I'd like to think I'd got a lot more than." (Interview 5)

I: "And if your friend had said it's fantastic, but you'd got this bad report, who would you have trusted?

R: I would have trusted her, but I would also everyone's different and our bodies are all different so I think I would have probably gone in the middle and my expectations would have been a bit of both." (Interview 1)

And with a positive outcome:

"R: Well I trust him, I'd believe him.

I: You'd believe it?

R: I'd believe him because I wanted to." (Interview 8)

This has implications for the implementation of such a tool, which will be explored in the discussion. The reason an outcome prediction tool has been allocated as a research priority by NICE is the high dissatisfaction rate. It is in this group that the tool would be most useful as it would alter expectations in line with predicted outcome and (hopefully) result in improved satisfaction (although this relationship has been questioned).[41] However, what I have found here is that although patients would alter their expectations, they would not alter their expectations all the way towards a "bad" prediction. This is likely to dampen the effect on satisfaction an outcome prediction tool could have. Additionally, any uncertainty in the prediction provided by a tool (as there will be with any prediction) is likely to be met with an optimistic view from patients – patients will view themselves at the better end of any confidence interval. This has implications for deciding how good a prognostic model has to be for it to be considered useful for individual patient decision-making. Given the optimism bias, any prognostic model will have to have more precise estimates if the aim is to aid patient decision-making (particularly for patients who are at risk of a poor outcome).

4.5 Discussion

This study has demonstrated that the effects of an outcome prediction tool on patients decision-making is likely to depend on their stage of decision-making (deliberation or decision-making), and that the effects of a poor outcome prediction are likely to be blunted by the optimism bias. This has broad implications for any future outcome prediction tool, one of which is the precision of individual estimates. If patients tend to think their outcome will be better, then they will assume they will fall into the better end of any confidence interval around a prediction – this means that estimates with a large individual confidence interval may not be particularly useful. Linked to this is the preference for information from friends and family. Conflicting information from a prediction and a family member who has had the operation is likely, and it appears that patients would prefer to hear from someone who has been through the procedure. This may mean that a completely different approach to presenting information is required: for example, a database of patient experience from patients that have had a knee replacement that can be matched to the baseline characteristics and likely outcome of a patient considering a knee replacement. Additionally, the effect of a tool on managing expectations and patient decision-making will alter depending on the point in the pathway it is used (patients who have already made up their mind appear less willing to change it based on new information – this could be due to the stress that is felt from the deliberation process, discussed in chapter 3). However, it is clear that patients welcome such information, and that it would appear to still have an effect on expectation and decision-making, especially if targeted early in the patient pathway.

The strengths and weaknesses of this study are similar to that of the study presented in Chapter 3. This study included people at various stages of decision-making, had a broad based research team, and a range of ages, ethnicities and genders. The methodology included techniques to improve the trustworthiness of the study. However, the same weaknesses regarding selection bias, comparison of views across research methods, and power differentials between participants and interviewers exist.

This study is the first of its kind to examine outcome prediction in this way; however, a wealth of information is available on information-giving strategies. Patient Decision Aids

(PDA, also known as decision aids, decision support interventions, decision support aids) are methods of informing patients about the treatment options available to them.[42] From a simple one-page summary to interactive online tools, they have been widely implemented within the NHS, with the Department of Health QIPP programme funding the development and hosting of 38 PDAs to cover a variety of conditions. Knee OA is included.[46] These aids are quite different from individualised prediction of outcome, particularly outcome based on predominantly psychological factors, and do not offer any potential for interventions based on predicted scores. However, the principle of patients weighing up probabilistic information is broadly similar.

A recent Cochrane review on the effectiveness of decision aids[45] concluded that in general they:

- Improve patients' knowledge of the options (high-quality evidence);
- Allow patients to feel more informed and more clear about what matters most to them (high-quality evidence);
- Allow patients to have a more accurate expectations of possible benefits and harms of their options (moderate-quality evidence); and
- Allow patients to participate more in decision-making (moderate-quality evidence).

Interestingly decision aids have been found to reduce the proportion of people progressing to elective surgery.[42,45] Although these studies did not involve patients with knee OA, there are similarities in that it is a preference-based decision.[42] There is, however, a caveat with informed decision-making – patients who have knee OA tend to prefer a paternalistic interaction, commonly viewing anything else as an attempt to avoid responsibility,[47-49] and shared decision-making models have been shown to have mixed effects on *clinical* outcomes (rather than outcomes aimed at measuring the decision-making process itself).[52]

These findings are largely consistent with our own, and are particularly relevant when considering how an outcome prediction tool should be used. It is clear that the effect of an outcome prediction tool is to a degree dependent on the content and presentation, the point in the pathway it is used, and whether it is delivering "good" or "bad" news. The work on PDAs would suggest a decrease in the proportion of people progressing to elective surgery could be expected. Additionally, how the tool is delivered is likely to be key (i.e. as part of a shared decision-making model or part of a paternalistic model). These uncertainties will need careful evaluation if and when such a tool becomes available.

4.6 Conclusion

This study has demonstrated that any prediction tool aimed at improving patients' decision-making will need to have precise estimates, and the timing of delivery of predictive information will alter the effects of any future tool capable of predicting outcome. The implications from this, in the authors' opinion, is that the timing and effect (both in terms of decision-making and clinical outcome) will have to be carefully evaluated for any potential outcome prediction tool that is to be used by patients.

With an understanding of the decision-making process, the potential effects of an outcome prediction tool, and patients' preferences regarding outcome prediction, an understanding of the potential factors that could affect outcome in knee replacements is required. The next chapter investigates this.

Chapter 5: The important factors to investigate to build an outcome prediction algorithm

This chapter will first examine what factors could be important in predicting outcome. It will then go on to a systematic review examining what patient factors should be measured when developing a study to quantify the relationship between pre-operative factors and outcome. This review was conducted in 2012, and was used to inform the development of the protocol for the multicentre Knee Outcome Prediction Study, described in chapters 6 and 7. A narrative update on important developments since 2012 is provided.

5.1 Declarations

Aspects of this chapter have been published:

T. Barlow, T. Clarke, M. Dunbar, A Metcalfe, D. Griffin. The effect of expectation on satisfaction in total knee replacements: a systematic review. Accepted for publication SpringerPlus, February 2016

Aspects of this chapter have been presented at an international conference:

Dunbar M, **Barlow T**, Griffin D. The effect of patient factors on outcome in Total Knee Replacement: a systematic review. Poster. European Federation of National Associations of Orthopaedics and Traumatology, Istanbul, June 2013.

Aspects of this chapter have been presented at a regional conference

T. Barlow, T. Clarke, M. Dunbar, A Metcalfe, D. Griffin. The effect of expectation on satisfaction in total knee replacements: a systematic review. Poster. West Midland Surgical Society Autumn meeting, Coventry, November 2015.

Dr M Dunbar and Dr T Clarke provided independent assessment of references for the systematic reviews on patient factors and expectations respectively.

Aspects of this review were conducted before registration for the degree of PhD. The work accounted for no more that three months full time equivalent.

5.2 Introduction

The development of an outcome prediction tool requires an understanding of the potential factors that could influence outcome. Therefore the following section describes previous attempts at identifying risk factors before reporting a systematic review of patient factors that could act as prognostic factors. The result of this review, completed in 2012, formed the basis for the design of the cohort study and is presented in its original form to provide context for chapters 6 and 7. The aim of this review was to identify factors that could be important in predicting outcome, rather than attempting to quantify those relationships through meta-analysis. To provide an account of the literature to date, a further narrative review on updates since 2012 is included.

5.2.1 Previous attempts at identifying risk factors

Many studies on knee replacement have explored the effect of different surgical techniques or rehabilitation on outcome. However, this has been unable to account for all of the variability in outcome. Using data from the NJR, Baker et al. analysed surgical factors that could account for variability in Oxford Knee Score (OKS) and EuroQol 5 Dimensions (EQ 5D).[95] This found that implant brand and hospital type were significant predictors, although they found that the difference was small, and the variation within each brand and hospital was large. Patient factors, which can be defined as being any factor that is intrinsic to the patient and that is not rapidly changed by a change in environment, had larger effect sizes.[98] More recently, the NIHR supported a Programme Grant examining risk factors for a poor outcome in joint replacement (the Clinical Outcomes in Arthroplasty Study – COASt). This study focused on peri-operative factors, not specifically patient factors, and concluded in August 2012 that "Other predictive factors need to be identified to improve our ability to recognize patients at risk of poor TKR [Total Knee Replacement] outcomes".[22] Additional aspects of peri-operative care have been investigated and found little effect on outcome: for example excision of the patella fat pad,[99] mobile or fixed bearing implants,[100] and computer navigated or conventional techniques.[101]

One factor that had not been studied in depth was the alignment of the knee prosthesis. Two systematic reviews, of which I am the second author, investigated the effect alignment has on either PROMs or revision rates after knee replacement. Both found that alignment has little effect on outcome, but the studies examining the issue were marred by several issues – not least of which was the complex interplay between the alignment of two different prosthesis (tibial and femoral) in three dimensions. Additionally, samples were not particularly representative, and attempts to control for baseline demographics were poor in most studies.[102] Therefore a further study, using the population of patients described in chapter six, was used to investigate the link. I am the senior author on this paper and it found no link between malalignment and six month OKS score (prepared for publication).

Therefore, if the surgical procedure itself was only accounting for a small proportion of the variability (around 15%),[22] other factors within the process should account for the variation in outcome.

5.2.2 Patient factors

There is growing evidence that patient factors significantly affect outcome.[89] A patient factor can be defined as being any factor that is intrinsic to the patient and that is not rapidly changed by a change in environment. These factors may include demographic data such as age, gender, and socioeconomic class, functional and general health scores, as well as psychological attributes and radiographic appearances.

Therefore, this review will systematically determine which pre-operatively measurable patient factors are associated with post-operative changes in status as measured by patient-derived and functional outcomes scoring in patients who are about to undergo total knee replacement for OA. The implications this has for the development of methods to identify patients likely to have poorer outcomes will be discussed.

5.3 Systematic review – Patient factors that influence outcome

This review was informed by a previous review performed by one of my supervisors.[98] I defined and conducted the search, assessed papers for inclusion, performed data extraction, and collated the results.

5.3.1 Patients and Methods

Search strategy

A comprehensive electronic search strategy was used to identify studies from MEDLINE (Medical Literature Analysis and Retrieval System Online, Bethesda, Maryland, USA) and EMBASE (Excerpta Medical Database, Amsterdam, The Netherlands) using all available data from their inception until February the 15th 2012.

The search strategy is available in the appendix (section IV) and online via the Prospero website.[103] It was designed to be as comprehensive as possible in order to mitigate the risk of producing 'precise but spurious results.'[104]

Eligibility criteria

Studies were eligible for inclusion if they were prospective cohort studies observing the effect of knee replacement on OA. Studies where information was retrieved from a database were also included if the pre-operative status patient factor measurements were collected prospectively. Case series and case-control studies were not included as there is a significant potential for selection bias with these types of study design.[105] Only studies that were presented in English were included in the analysis.

The subjects included in each study were patients about to undergo total knee replacement with a diagnosis of OA. Where patients with other arthritic diseases (e.g. traumatic arthritis, inflammatory arthritis) made up more than 5% of the study population, these studies were excluded. Studies where the cohort comprised more than 5% of patients undergoing revision knee replacement were also excluded from the analysis. This figure was agreed by the study group and included in the published protocol. However, studies containing mixed groups of patients were included if there was subgroup analysis that clearly differentiated the population of interest; when this occurs, only the results from the subgroup are discussed.

Any study that collected information on patient factors retrospectively was excluded as this has been shown to be unreliable.[106]

Patient measurements

All measurements of patient functional status, psychological factors and radiological measurements had to have been made using methods that had evidence of validity for patients with severe knee OA.

All outcome measurements had to have been made using validated patient reported outcome measurement tools. This method of measurement has been shown to have good validity and reliability with a significant reduction in the likelihood of assessor bias.[107] This meant that the historically popular Knee Society Score (also known as the American Knee Score or Knee Society Clinical Rating Scale)[108] was not included as it has several components that require objective assessment by an observer. The Knee Society Score has been shown to have poor correlation amongst its items when compared with other more recently developed patient reported tools.[109]

A minimum period of follow up of three months was required.

Analytic methods

Studies had to have made some attempt to associate outcome with one or more of the measurable patient factors. Various methods of regression or correlation analysis were acceptable as long as they were clearly explained in the methods section in order to determine that their use was appropriate for the type of data collected.

Quality assessment

The Newcastle Ottawa scale provides a system for assessing quality across three domains: selection, comparability, and outcome.[110] The Newcastle-Ottawa Scale (NOS) is a tool developed through the Delphi process by the Universities of Newcastle, Australia and Ottawa, Canada. It was developed to allow a framework for assessing the quality of case-control and cohort studies (each framework differs slightly). For cohort studies, the quality of studies is judged under three broad categories: Selection, Comparability, and Outcome. Each domain is scored with a star rating system. Face validity and inter-rater reliability have been demonstrated, with more validation work currently ongoing.[111] The score is easy to use, allows quick comparison between studies, and is consistent between raters, hence its use here.

However, there has been some criticism of the score within the literature, due to the subjectivity of some of the elements within the scoring system.[110] With over 86 tools available for the quality assessment of non-randomised controlled trials, it is clear that no tool is perfect.[110] However, guidelines on the conduct of systematic reviews state that a scoring system should be used.[110] The caveat to using such a system is the inappropriate weighting of studies and the subsequent production of spurious results. A summary score is not provided in line with the scoring system guidelines.[110]

Data extraction

After the initial search was performed the studies were screened for eligibility in sequential rounds where their relevance was assessed using at first their titles, then abstracts, and finally full review of the paper. Mark Dunbar acted as the second author, and independently re-examined each paper at each stage to ensure that they met the inclusion criteria. Relevant data was extracted and a quality assessment performed independently by both reviewers, resolving any differences through discussion and review.

Due to the nature and heterogeneity of the analyses used in the studies no formal meta-analysis was performed. Instead, a narrative approach was taken which still allowed comparison of individual important factors across all studies. This is consistent with the aim of this review: to identify potential predictors of outcome.

5.3.2 Results

Our search returned 2287 studies. Of these some were duplicates from multiple databases that due to a technical limitation had to be removed by hand during the title search. Figure

5 is a flow chart detailing the studies that were excluded. Twenty-two studies are included in this review (Table 7).

Table 7: Studies included in review (continued until page 118)

Author	Year	Title	Patients Included	Patients Lost to Follow up	Follow up length	Primary Outcome	Secondary Outcome	Analysis	Sample Size Calculation
Sharma et al.	1996	Prognostic factors for functional outcome of total knee replacement: a prospective study	52	5	3 months	SF-36 PF	na	Hierarchical multiple regression	Not reported
Heck et al.	1998	Patient outcomes after knee replacement	291	22	2 years	Dichotomised SF-36 PF	Womac (not included in regression model)	Logistic Regression	Not reported
Fortin et al.	1999	Outcomes of total hip and knee replacement: pre-operative functional status predicts outcomes at six months after surgery	130	24	6 months	SF-36	WOMAC	Multiple linear regression	Not reported
Kiebzak	2002	The SF-36 general health status survey documents the burden of OA and the benefits of total joint arthroplasty: but why should we use it?	415	None mentioned	1 year	SF-36	na	Friedman test; Mann Whitney test	Not reported
Allyson Jones et al.	2003	Determinants of function after total knee arthroplasty	294	18	6 months	SF-36	WOMAC	Stepwise multiple regression	Not reported
Lingard et al.	2004	Predicting the outcome of total knee arthroplasty	860	119	1 year	SF-36	WOMAC	Hierarchical multiple regression	Not reported

Table 7 (cont.)

Author	Year	Title	Patients Included	Patients Lost to Follow up	Follow up length	Primary Outcome	Secondary Outcome	Analysis	Sample Size Calculation
Mizner et al.	2005	Pre-operative quadriceps strength predicts functional ability one year after total knee arthroplasty	40	0	1 year	Timed up and go and stair climbing test	KOS/ADLS and SF-36 PCS	Hierarchical linear regression	Not reported
Lim et al.	2006	The effect of pre-operative symptom severity on functional outcome of total knee replacement - patients with the lowest pre-operative scores achieve the lowest marks	45	0	2 years	OKS	na	Spearman rank; Wilcox signed rank	Not reported
Nunez et al.	2007	Health-related quality of life in patients with OA after total knee replacement: factors influencing outcomes at 36 months of follow-up	90	23	3 years	WOMAC	na	Multiple linear regression	Not reported
Bourne et al.	2007	Influence of patient factors on TKA outcomes at 5 to 11 years follow up	728	81	5 years	WOMAC	SF-12, KSS	ANOVA	Not reported
Escobar et al.	2007	Effect of patient characteristics on reported outcomes after total knee replacement	907	640	6 months	Each domain of the WOMAC and SF-36	na	Multiple linear regression	Not reported
Cushnaghan et al.	2008	Long-term outcome following total knee arthroplasty: a controlled longitudinal study	657	332	6 years	SF-36 (PF change score only used for analysis)	None	Linear regression	Not reported

Table 7 (cont.)

Author	Year	Title	Patients Included	Patients Lost to Follow up	Follow up length	Primary Outcome	Secondary Outcome	Analysis	Sample Size Calculation
Davis et al.	2008	Effects of socioeconomic status on patients' outcome after total knee arthroplasty	974	181	24 months	WOMAC PF, WOMAC pain	None	Multivariate linear regression	Not reported
Franklin et al.	2008	The Chitranjan Ranawat Award: functional outcome after total knee replacement varies with patient attributes	9220 on registry	1170	12months	KSS	Sf-12 (PCS and MCS)	Multivariate regression analysis	Not reported
Rajgopal et al.	2008	The impact of morbid obesity on patient outcomes after total knee arthroplasty	760 on registry	210	12 months	WOMAC	SF36	Linear regression. T test to compare BMI groups.	Rule of thumb of 10 patients per variable (6 variables included in model)
Nilsdotter et al.	2009	Knee arthroplasty: are patients' expectations fulfilled? A prospective study of pain and function in 102 patients with 5-year follow-up	102	22	5 years	KOOS	SF-36, ADL and Leisure activities (KOOS), Satisfaction	Mann Whitney U test	Not reported
Nunez et al.	2009	Total knee replacement and health-related quality of life: Factors influencing long-term outcomes	142	30	7 years	WOMAC	SF-36 (not included in regression model)	Multiple linear regression	Not reported

Table 7 (cont.)

Author	Year	Title	Patients Included	Patients Lost to Follow up	Follow up length	Primary Outcome	Secondary Outcome	Analysis	Sample Size Calculation
Dowsey et al.	2010	The impact of pre-operative obesity on weight change and outcome in total knee replacement: a prospective study of 529 consecutive patients	529	8	12months	Weight change	SF12 - PCS and MCS, (KSS)	Kruskal Wallis tests	Not reported
Ghandi et al.	2010	Metabolic syndrome and the functional outcomes of hip and knee arthroplasty	889 on registry	222	12months	WOMAC	na	Linear regression	Not reported
Lopez-olivio et al.	2011	Psychosocial determinants of outcomes in knee replacement	272	31	6 months	WOMAC	KSRS	Multiple linear regression	80% power to detect a cumulative R2 as small as 0.067 with 10 independent variables.
Nunez et al.	2011	Factors influencing health-related quality of life after TKA in patients who are obese	63	3	12 months	WOMAC	na	Linear regression	Not reported
Clement et al.	2012	The outcome of primary total hip and knee arthroplasty in patients aged 80 years or more	677 total (185 cases >80, 492 controls <80)	None mentioned	12 months	OKS	SF-12, Satisfaction	Mann Whitney U test	Not reported

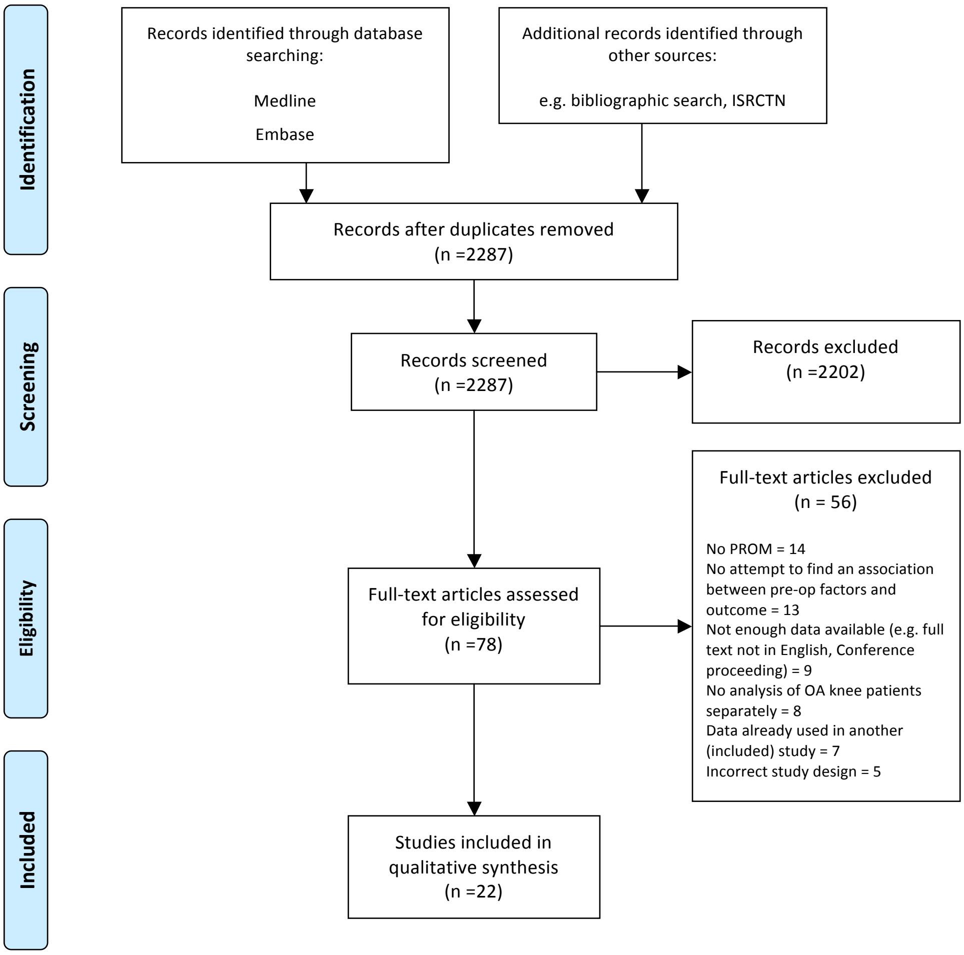


Figure 5: Flow diagram of included studies. Adapted from Moher et al.[66]

Quality assessment

Table 8 describes the quality assessment using the Newcastle Ottawa scale. The quality of studies is judged under three broad categories: Selection (maximum four stars), Comparability (maximum two stars), and Outcome (maximum 3 stars).

Table 8: Quality Assessment (NOS)

Author	Year	Selection	Comparability	Outcome
Sharma et al.	1996	3	0	2
Heck et al.	1998	3	0	3
Fortin et al.	1999	3	0	2
Kiebzak	2002	3	0	2
Allyson Jones et al.	2003	3	0	1
Lingard et al.	2004	3	2	3
Mizner et al.	2005	3	1	2
Lim et al.	2006	2	0	2
Nunez et al.	2007	3	0	2
Bourne et al.	2007	3	0	2
Escobar et al.	2007	4	2	2
Cushnaghan et al.	2008	4	1	2
Davis et al.	2008	4	2	3
Franklin et al.	2008	4	2	2
Rajgopal et al.	2008	4	2	2
Nilsdotter et al.	2009	3	2	3
Nunez et al.	2009	4	0	3
Dowsey et al.	2010	4	2	3
Ghandi et al.	2010	4	2	3
Lopez-olivio et al.	2011	4	1	3
Nunez et al.	2011	4	0	3
Clement et al.	2012	4	0	3

Outcome measures

Various outcome measures were used including:

- OKS – a 12 item, 5-point Likert scale questionnaire. Higher scores reflect better pain and/or function in the knee. This is the PROM used by the DoH. It has been well validated for patients undergoing knee replacement.[17,112]
- WOMAC – the WOMAC measures five items for pain (score range 0–20), two for stiffness (score range 0–8), and 17 for functional limitation (score range 0–68). Total range of 0-96 with higher scores being worse. It is well validated for this group of patients.[113]
- KSRS – A combination of assessment of instability, pain, range of motion, and patient function. This system has PROM and physician assessment. Higher sores indicate a better functioning knee (continuous variable).[108]
- KSS – Assessment identical to the KSRS; however there is not assessment of patient function.[108]
- KOOS – Likert scoring system over 5 subscales (pain, other symptoms, Activities of Daily Living (ADL), sports and recreational activities, and knee related quality of life) producing a continuous score from 0 (extreme symptoms) to 100 (no symptoms).[113]
- SF-36 – a 36-item general health.[114] The SF-36 measures eight domains of health, which can used to produce summary scores for Physical and Mental domains. It is a continuous variable with higher scores reflecting better health. The SF-12 is a shorter, 12-item version.

Candidate predictors

Table 9 displays the relationship between patient factors and outcome. This table has been produced so that any statistically significant associations can be seen. Of note, where a study provided univariate and multivariate analysis, only the results of the multivariate analysis are included in the table.

In brief, factors that have clearly been associated with a poor outcome include:

- Worse pre-operative knee function scores;[90-94,115-120]
- Psychosocial factors including decreased social support, more depression, decreased ability to cope, and various general measures of mental health;[90,92,94,119,120]
- A higher number of other joints affected (joint co-morbidity);[118,119]
- Certain anthropomorphic measurements designed to identify short, thick legs.[121]

Factors that have been inconsistently linked with outcome include:

- Medical co-morbidity has, in some studies, been associated with a worse post-operative function,[92,115,120,121] although other studies of reasonable size have not found a correlation;[90,91,118,122-124]
- BMI has been associated with worse outcome,[92,94,117,123,125] and more complications,[125] however several studies have found no correlation;[115,118-120,122]
- Some studies have demonstrated no difference in outcome with female gender,[90,91,94,115,119,120,122] however, four large cohort studies have found a correlation, suggesting that female gender is a predictor of poor functional outcome following surgery;[92,118,123,126]

- Some studies have demonstrated increasing age is not associated with outcome,[91,117,119,120,122], several large studies have found a correlation with worse outcome, [92,94,115,118,127], with one study finding an association with better outcome (however, this study dichotomised the SF-36 PCS).[90]

Education, smoking, ethnicity, quadriceps strength, and income had either non-significant results, or produced correlations that were too small to be of clinical significance.

Table 9: Factors associated with outcome in knee replacement **(continued to page 128)**

Author	Age	Gender	BMI	Knee function	Comorbidities	Psychological measures	Other
Sharma et al., 1996	Increasing age not associated with SF-36 PF (p=0.874)	Gender not associated with SF-36 PF (p=0.083)	Increasing BMI not associated with SF-36 PF (p=0.805)	Physical function (PF domain of SF-36) not associated with SF-36 PF (p=0.103)	Increasing numbers of comorbidities not associated with SF-36 PF (p=0.053)	Social function was associated with SF-36 PF (p=0.027), but Role functioning emotional (p=0.06) and Motivation (p=1.64) were not	Lower level of education (p=0.119), quadriceps strength (p=0.788) and social support (p=0.466) were not associated with SF-36 PF
Heck et al.,1998	Increasing age associated with better SF-36 PF* (OR 1.09)	Gender not associated with SF-36 PF	-	Baseline WOMAC associated with better SF-36 PF (OR = 1.1)	Comorbidities not associated with SF-36 PF	Better pre-operative SF-36 MF predicted better SF-36 PF (OR = 1.11)	-
Fortin et al., 1999	Age not associated with SF-36 PF, WOMAC Pain, or WOMAC Function	Gender not associated with SF-36 PF, WOMAC Pain, or WOMAC Function	-	Better SF-36 PF associated with better SF-36 PF post-operative (0.36+/- 0.13) and better WOMAC function (0.61+/- 0.11)	Comorbidities not associated with SF-36 PF, WOMAC Pain, or WOMAC Function	-	Lower level of education not associated with SF-36 PF, WOMAC Pain, or WOMAC Function
Kiebzak et al., 2002	-	Female gender associated with worse SF-36 (p<0.04)	-	-	-	-	-
Allyson Jones et al., 2003	Increasing age associated with worse WOMAC function (p=0.05; 0.35+/-25), but not with SF-36 PF (p=0.12)	Female gender not associated with WOMAC (p=0.91) or SF-36 PF (p=0.39)	Increasing BMI not associated with WOMAC or SF-36.	WOMAC associated with better WOMAC (p<0.001; 0.3 +/-0.13) and SF-36 (p<0.001; 0.36+/-0.09)	Increasing number of comorbidities associated with worse WOMAC function score (p=0.005; 1.62+/-1.13) but not pain score	-	-

**This result represents a logistic regression on a dichotomised SF-36 PCS*
OR = Odds ratio. P values combined with model coefficients and 95% confidence intervals (in parenthesis) are given when they were reported. Values are for the results of multiple regression models when this was conducted, or univariate models when no multivariate model was performed.

Table 9 (cont.)

Author	Age	Gender	BMI	Knee function	Comorbidities	Psychological measures	Other
Lingard et al., 2004	Increasing age associated with worse SF-36 PF	Female gender associated with worse WOMAC pain, but not function.	Higher BMI associated with worse SF-36 PF, not MF or WOMAC	Better baseline WOMAC and SF-36 associated with better WOMAC and SF-36 PF	Increasing number of co-morbidities associated with worse SF-36 PF; not MF or WOMAC	Better pre-operative SF-36 MF predicted better SF-36 PF and better WOMAC	
Mizner et al., 2005	Increasing age not associated with SF-36 PCS	-	-	-	-	-	Quadriceps' strength not associated SF-36 PCS
Lim et al., 2006	-	-	-	Better pre-op OKS associated with better OKS (P=0.017)	-	-	-
Nunez et al., 2007	Increasing age not associated with WOMAC	Gender not associated with WOMAC	Severe (Class III) obesity (BMI 35-39.9 kg/m2) was associated with more WOMAC pain (P=0.049), but not function	Not reported	-	-	-
Bourne et al., 2007	Patients over 80 years of age had lower (p 0.01) WOMAC (Univariate)	Not significant (Univariate)	Not significant (univariate)	Not reported	-	-	-

OR = Odds ratio. P values combined with model coefficients and 95% confidence intervals (in parenthesis) are given when they were reported. Values are for the results of multiple regression models when this was conducted, or univariate models when no multivariate model was performed.

Table 9 (cont.)

Author	Age	Gender	BMI	Knee function	Comorbidities	Psychological measures	Other
Escobar et al., 2007	Increasing age associated with worse WOMAC pain (p=0.04) and stiffness (p=0.046) but not functional limitation (p=0.08;	Female gender associated with worse functional limitation (p=0.008) and stiffness (p=0.03) but not pain (p=0.06)	-	Better WOMAC associated with better WOMAC	Charlston index associated with WOMAC pain (p=0.005), functional limitation (p=0.008), but not stiffness (p=0.3)	Better pre-op SF-36 MH associated with WOMAC pain (p=0.001), functional limitation (p=0.005) and stiffness (p=0.03)	Low back pain associated with WOMAC pain (p<0.001), function (p=0.01), and stiffness (p=0.002) and lack of social support associated with WOMAC pain (p=0.02), function (p=0.002), but not stiffness (p=0.051). Better pre-op SF-36 domains associated with WOMAC pain, functional limitation, and stiffness
Cushnaghan et al., 2008	Age over 75 years associated with worse SF-36 PF (-9.1 (-16.9 to -1.2))	Female gender associated with worse SF-36 PF (-7.5 (-14.9 to 0.0)	BMI over 30 not associated with SF-36 PF (-4.6 (-14.5 to 5.3)	Better pre-op SF-36 PF associated with worse SF-36 PF change score (24.6 (26.3 to 22.9)**	Individual comorbidities not associated with worse SF-36 PF change scores	_	Joint comorbidity (joint count) predicted worse SF-36 PF (p=0.03); Smoking (-5.1 (-17.1 to -6.9) and pre-op radiological status (5.6 (-2.8 to 14.1) not associated with outcome.
Davis et al., 2008	_	_	_	_	_	_	Lower income was not associated with outcome (WOMAC 6 and 24 months) except for WOMAC Pain at 12 months (p=0.014) Education was not associated with WOMAC at any time point (p= 0.36-0.97)
Franklin et al., 2008	Age not associated with SF-12 PCS (p=0.073; model coefficient= -0.031 (-0.065 to 0.003)	Gender was not associated with SF-12 PCS (p=0.033)	Higher BMI was associated with worse SF-12 PCS (p=0.001; model coefficient =-1.068 (-1.689 to -0.447)	Better pre-op SF-12 PCS associated with worse SF-12 PCS change score** (p<0.001; model coefficient=-0.844 (-0.903 to -0.784)	_	Better SF-12 MCS was associated with better SF-12 PCS (p=0.01; model coefficient 0.038 (0.009 to 0.066)	_

***The SF-36 PF change score was used, rather than adjusting for the baseline score by using it as a covariate within the model. This suggests that the change score is lower for higher functioning individuals, but does not reflect the absolute score achieved.*

Table 9 (cont.)

Author	Age	Gender	BMI	Knee function	Comorbidities	Psychological measures	Other
Rajgopal et al., 2008	Age not associated with WOMAC (p=0.967; model coefficient= 0.004 (-0.169 to 0.176)	Gender not associated with WOMAC (p=0.279; model coefficient not displayed as no reporting on reference group)	BMI over 40 associated with worse WOMAC (p=0.027; model coefficient= -5.188 (-9.711 to -0.606)	Better baseline WOMAC associated with better WOMAC (p<0.001; model coefficient =0.301 (0.202 to 0.399)	Worse Charnley Hip grade had worse post-operative WOMAC (p=0.012; model coefficient = -4.897 (-8.701 to -1.093)	Higher SF-12 MCS associated with higher WOMAC (p=0.005; model coefficient = 0.210 (0.063 to 0.357)	Prior contralateral TKA made no difference to one year WOMAC (p=0.279; model coefficient = 3.157 (-2.487 to 8.8))
Nilsdotter et al., 2009	_	_	_	_	_	_	Expectation not associated with KOOS (univariate)
Nunez et al., 2009	_	Female gender associated with worse WOMAC function (p=0.015; model coefficient = 14.4 (2.8 to 25.9)) WOMAC stiffness and pain not reported	BMI over 35 associated with worse WOMAC pain (<0.001; model coefficient = 9.7 (4.3–14.4)), function (p=0.042, model coefficients = 5.4 (0.3 to10.8))	Baseline WOMAC not associated with WOMAC domains.	Number of comorbidities not associated with WOMAC	_	_
Dowsey et al., 2010	_	_	Non-obese and obese had improved outcomes compared with morbidly obese patients in 12 months SF-36 PF (p = 0.05)	_	_	_	_

OR = Odds ratio. P values combined with model coefficients and 95% confidence intervals (in parenthesis) are given when they were reported. Values are for the results of multiple regression models when this was conducted, or univariate models when no multivariate model was performed.

Table 9 (cont.)

Author	Age	Gender	BMI	Knee function	Comorbidities	Psychological measures	Other
Ghandi et al., 2010	Age not associated with WOMAC	Gender not associated with WOMAC	A diagnosis of obesity resulted in worse WOMAC scores (p=0.04; model coefficient = 3.6 (0.02, 7.2)	Not reported	Increasing number of Metabolic Syndrome comorbidities (BMI > 30 kg/m2, diagnosis of hypercholesterolemia, hypertension, or diabetes) was associated with worse WOMAC (pain (p=0.02; function, p=0.006)	_	_
Nunez et al., 2011	-	-	-	-	Increasing number of comorbidities associated with worse WOMAC scores (p=0.012)	-	Ratio of length to girth of leg associated to WOMAC score (i.e. short, fat legs associated with worse WOMAC pain (p=0.021) and function (p=0.023)
Lopez-olivio et al., 2011	-	-	Increased BMI was not associated with WOMAC function (p=0.5; model coefficients = 0.1 (0.05) or pain (p=0.07; model coefficients = 0.3 (0.11))	Better baseline WOMAC associated with better WOMAC pain (p<0.001; model coefficients = 0.2 (0.25))	Increasing number of comorbidities associated with worse WOMAC pain score (p=0.008; model coefficient = 3.0 (0.17), but not function score (p=0.06; model coefficient = 0.6 (0.04)).	Increased social support (p=0.01; model coefficient = −2.7 (−0.15)), less depression (p=0.02; model coefficient = 0.4 (0.15)), and increased ability to cope (p=0.01; −5.3 (−0.20)) predicted better WOMAC function.	Less education predicted worse WOMAC pain (p=0.01; model coefficient = −1.6 (−0.17). Ethnicity was not associated with WOMAC (p>0.3, univariate).

OR = Odds ratio. P values combined with model coefficients and 95% confidence intervals (in parenthesis) are given when they were reported. Values are for the results of multiple regression models when this was conducted, or univariate models when no multivariate model was performed.

Table 9 (cont.)

Author	Age	Gender	BMI	Knee function	Comorbidities	Psychological measures	Other
Clement et al., 2012	Patients over 80 were associated with worse 12 month SF-12 PCS (p=0.04), but not OKS (p=0.16) or SF-12 MCS (p=0.49)	–	–	–	–	–	–

OR = Odds ratio. P values combined with model coefficients and 95% confidence intervals (in parenthesis) are given when they were reported. Values are for the results of multiple regression models when this was conducted, or univariate models when no multivariate model was performed.

The aim of this review was to identify prognostic factors that could be tested within a cohort study in the production of a prognostic model. Therefore, any factor that had evidence of an association was relevant: a graphic representation of the candidate patient factors identified in this review, and the number of studies demonstrating an association with those factors, is displayed in Figure 6. Figure 7 is an identical chart, demonstrating the number of patients.

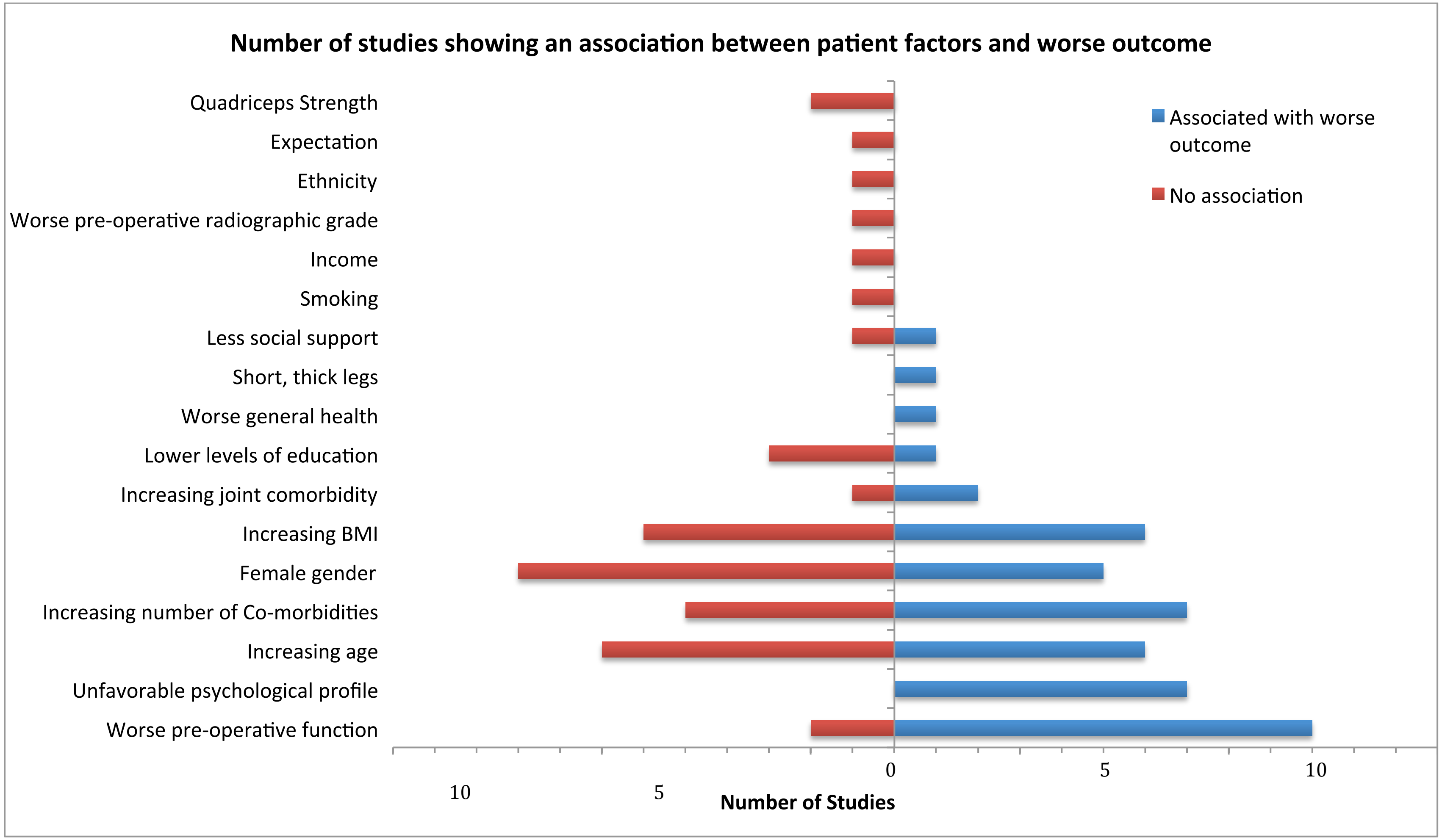


Figure 6: Number of Studies demonstrating an association between patient factors and PROMs. One study found an association between improved SF-36 PCS and increased age; however, it dichotomised the SF-36 outcome measure and has not been displayed. This figure does not represent any pooled estimates (i.e. meta-analysis).

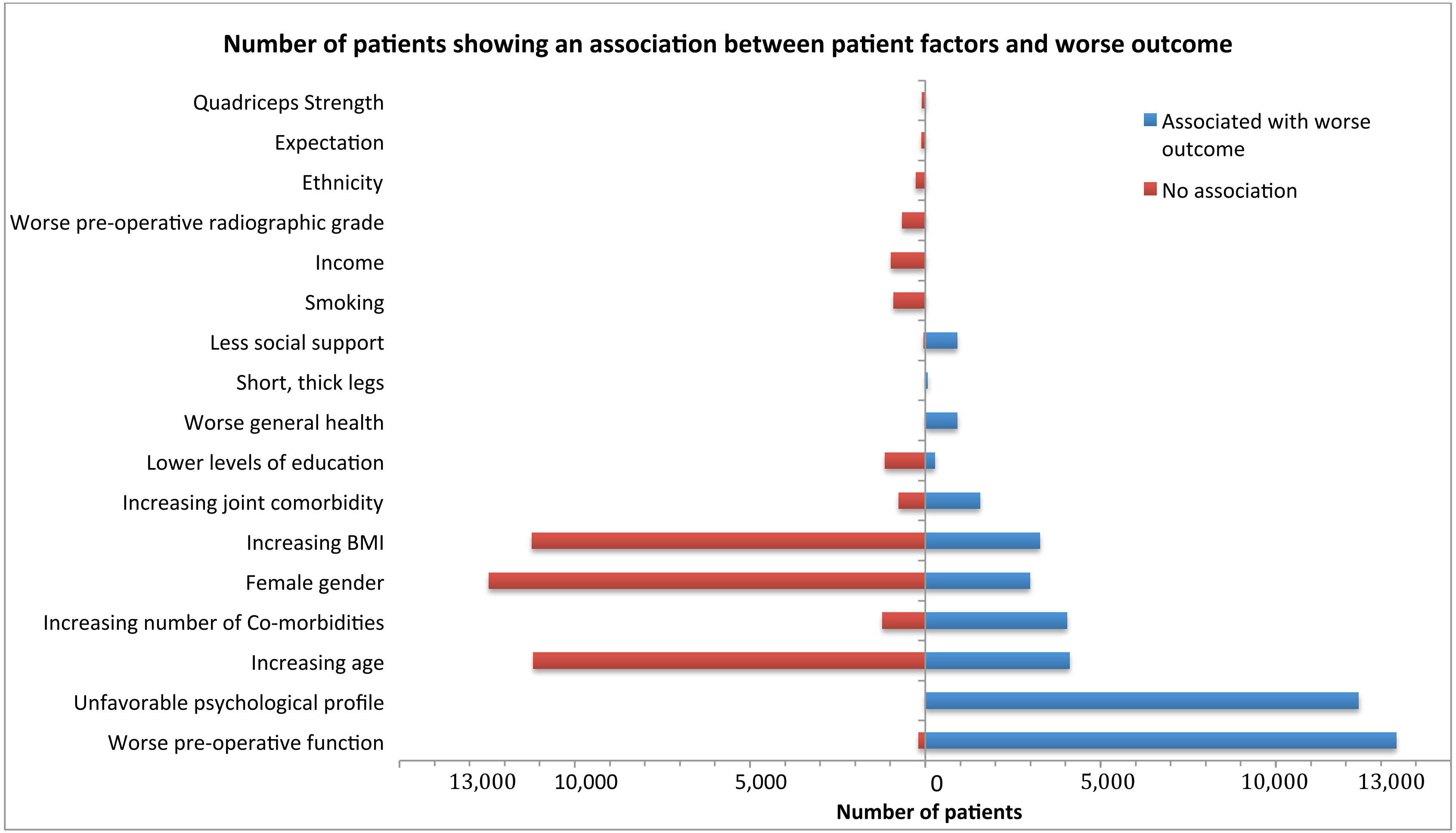


Figure 7: Number of patients in studies demonstrating an association between patient factors and PROMs. One study found an association between improved SF-36 PCS and increased age; however, it dichotomised the SF-36 outcome measure and has not been displayed. This figure does not represent any pooled estimates (i.e. meta-analysis)

5.3.3 Discussion

Functional Findings

The strongest and most consistent associations were between pre-operative knee status and post-operative knee status: those with higher pre-operative function had higher post-operative function. However, the Cushnaghan paper that reviewed change scores found a lower change score for those with higher pre-operative knee status suggesting that patients with lower pre-operative scores achieve lower absolute post-operative scores, but achieve more health gain (as measured by the change score in the PROMs). This finding has been supported by a recent paper by Judge.[26] However, PROMs scores are not linear in their measurements, and different health gains will mean different amounts to each patient.

What is yet to be clarified is how the improvement in knee status relates to the patient's perception of their outcome. This has been explored within the issues of patient satisfaction, but so far there are no robust definitions of this term and also no reliable tools available for its measurement. However, it does highlight the issue of value judgements that patients make; in particular to knee replacements, the judgement about the timing of the surgery may be relevant as patients with lower knee status may well also have lower expectations and demands from their surgery leading to a better perception of outcome.

Demographic Factor Findings

Age, gender and BMI demonstrated associations in several of the larger cohorts with no significant findings in all of the smaller studies. All but one study[118] looked at absolute scores as opposed to change scores. In general, the trend was towards worse outcomes for increasing age, female gender and a higher BMI; however, the size of these changes means that the clinical importance in questionable.

Psychological Factors Findings

The influence of psychological factors was only studied in six of the included papers, but in each one there was a significant association in the direction of improved psychological scores being associated with better outcomes. In the past the measurement of psychological factors have been restricted to general mental health or levels of anxiety and depression. With the increased popularity of practical psychometric tools that can explore dimensions outside of traditional depression, a marked increase in the number of significant explanatory factors can be expected.

The notion of modifying psychological attributes and the effect of this modification on outcome is an interesting avenue that requires further exploration.

Review limitations

The aim of this review was to identify candidate prognostic factors that could be tested within a cohort study in the production of a prognostic model. Therefore, any factor that had evidence of an association was relevant. Formal meta-analysis was not required to meet the aim.

English language articles were specified in the inclusion criteria for full paper review, but not in the search strategy. So although the possibility of missing important information from other sources existed, in practice there were no fully published papers in other languages that would have met the inclusion criteria.

Several studies comprised only small numbers of patients (less than 300) and therefore may not have had the power to detect associations: for example, Sharma et al. included 52 patients in a regression model with 13 explanatory variables. There was a trend towards a greater number of associations amongst the larger studies.

Two papers that were not included in this review deserve mention. Sullivan et al. published a paper in 2011 that was not identified by our search criteria at the time, but has been identified running an identical search subsequently.[128] A possible reason for this is that there was a delay in indexing this article, which led to it being omitted from our search. This study examined 120 patients and found that pain catastrophising (rumination over pain and/or description of it in more exaggerated terms) was associated with outcome. The second paper, by Lingard et al. in 2007, used an identical population of patients to the paper by the same author included in the review.[129] This used the same data, but dichotomised the SF-36 scores into those who were psychologically distressed and those who were not. Psychological distress was associated with a worse outcome, consistent with their previous findings.

There was some variation in the length of follow up between studies. This has the potential to introduce a form of timing bias as it has been shown that the functional status of knees after replacement can improve for around 2 years following surgery, although patients tend to follow the same trajectory (i.e. patients with poorer outcomes at six months have poorer outcomes at one and two years).[130] Studies that did not show associations in some domains might well have done so if the length of follow up was extended.

Despite using similar outcome measures, the use of change scores in some studies as opposed to absolute scores has the potential to give rise to different degrees of association from the same population.[122] Overall, however, it was felt that the directions of these associations were similar.

Systematic reviews are always subject to publication bias and in particular the delay or lack of publication of studies with negative findings.[131] I tried to minimise this by including all archived, published research from each of our searched databases. This resulted in a large attrition rate from over 2000 papers down to 22, but the possibility remains that some evidence may remain unpublished. This is more likely from older, less well-designed studies, as the resources required performing a high quality modern, observational study would make publication more likely irrespective of the findings.

Finally, in some studies the parameter estimates of significant candidate factors were so small that they were unlikely to represent clinically meaningful findings despite being statistically significant.

5.3.4 Summary

Only a few factors have been demonstrated to consistently affect outcome. These include pre-operative knee status, psychological wellbeing, social support and certain anthropometric measurements. There are issues with the quantification of the size of their influence.

To date no single study has sought to measure them all adequately. There is still a need for a well-powered study that uses tools with adequate resolution to investigate them, particularly psychological factors. The next Chapter details the development of a protocol for a multicentre cohort study designed to develop an outcome prediction tool for patients considering a total knee replacement, based on this systematic review.

However, as this systematic review was completed in 2012, an update on some of the important advances since then is described in the following pages.

5.4 Update on work since 2012

The review described previously formed the basis for the design of the cohort study and is presented in its original form to provide context for chapters 6 and 7. Since the completion of this review in 2012, there has been a plethora of work on pre-operative variables that could predict outcome in knee replacement, combined with examining variables over the entire patient pathway. This section details the results from individual, key studies and reviews on the topic to provide an up to date account of potential prognostic factors.

Expectations

The effect pre-operative expectations have on PROMs has been studied in detail. Most reviews have included both knee and hip replacements together,[132-134] but combining these operations is potentially flawed as they differ not only by outcome (and, one would expect, by pre-operative expectation),[17] but also by patient demographics and potentially aetiology.[58,59] The findings of these reviews are conflicting, potentially due to the combination of hip and knee replacements, to the different PROMs used, and different measures on expectation.

The effect of pre-operative expectations on satisfaction has also been studied. This has particular interest, as one of the potential effects of a predictive tool is to alter pre-operative expectations, and therefore potentially affect satisfaction rates by decreasing the number of patients with a mismatch between expected and actual results. To investigate this relationship I conducted a systematic review of the literature examining if pre-operative expectations were linked to post-operative satisfaction in total knee replacements. This review included only four papers and was again conflicting, demonstrating either small effects, or no effects. This was potentially due to every paper using a different measure of satisfaction and expectation, and one of the main findings from this paper was the inconsistency in measuring tools for both satisfaction and expectations.[41]

The inconsistency in measuring tools may be due to the difficulty in measuring constructs such as expectations and satisfaction. Multiple theoretical models exist to try and explain some of the complexity. For example the latent state-trait theory suggests that with measurement instruments we measure a person's state, which will depend upon the person (the person's traits), the situation (the state the person finds themselves in), and the interaction between the person and situation.[135] This highlights the difficulty in measuring these constructs consistently and accurately, and may go some way to explain the low numbers of studies examining this key issue. It seems likely that until the orthopaedic community can reach a consensus on what is important to measure, and how to measure it, progress will be slow.

There are other studies that suggest that expectation is related to outcome. Expectation fulfilment describes if a patients expectations have been met or not post-operatively.[136] As a post-operative measure, it is not useful in developing a prediction tool, but it is logical that patients whose expectations are not fulfilled are likely to be less satisfied. This would support the view that pre-operative expectations are related to satisfaction, as expectation fulfilment depends not only on the function and pain outcomes, but if that meets what the patient expected. The link between expectation fulfilment and outcome (function, pain and satisfaction) has been demonstrated in the literature,[136] suggesting that pre-operative expectations do indeed affect satisfaction. However, a further layer of complexity exists when the shift in patients' view of what is healthy or to be expected over the course of their treatment (response shift) is considered.[137] This means that what a patient expects changes over the course of their treatment, and therefore pre-operative expectations cannot be used as a measure of whether or not a patient's expectations have been met post-operatively (as they may have changed). What is clear from this body of work is that if a patient feels their expectations have been met (even if their pre-operative expectations have not been met) they are more likely to be satisfied.[136,138-140]

Psychological factors

In 2012 Vissers et al.l conducted a systematic review of psychological factors associated with outcome in knee replacement.[141] Results were similar to the review presented above, with poorer mental health, measured by the SF-12 or SF-36, demonstrating poorer pain and function outcomes. Pain catastrophisation was associated with more pain post-operatively; pre-operative depression and expectations had conflicting evidence of an effect on outcome. A systematic review and meta-analysis from Lewis et al. in 2014 examining factors that predicted persistent pain concluded that mental health and catastrophising predicted post-operative pain.[142] In 2012 Judge et al. reported on a cohort of almost 2000 patients, detailing that anxiety and depression were among the main determinants of outcome.[22] Clement also reported a paper detailing the improvement in mental health that patients experience over the course of a knee replacement.[143]

In 2015, Baert et al. conducted a review on the effect central modulation of pain has on outcome in knee replacement.[144] Central modulation was thought to occur via a biopsychosocial model – inherent to this is the proposition that altered inhibitory and facilitatory pain mechanisms lead to altered sensory processing in the brain. Emotions and cognitions can regulate pain pathways (so called "cognitive emotional modulation"). The review found three broad methods of testing for central modulation of pain: psychosocial variables (cognitive emotional modulation) as measured by questionnaires testing various psychological constructs (e.g. locus of control, depression, anxiety, catastrophising); clinical manifestations of altered central pain modulation (only one study examined this using pain at rest as representing altered central pain modulation); and quantitative sensory testing (using stimulation to test pain thresholds). For psychosocial variables the authors concluded that catastrophic thinking, poor coping strategies, and depression could affect outcome, whereas anxiety is unlikely to. Pain at rest is associated with worse pain post-operatively, although the authors point out that pain at rest may not be due to central sensitisation, but pain from structural factors in the joint itself. Pain threshold testing found that patients with lower pain thresholds pre-operatively had poorer pain outcomes.

Co-morbidities

In 2013, Clement et al. reported a study including over 2000 patients, where low back pain was an independent predictor of worse post-operative OKS and satisfaction,[145] and Lewis found that co-morbidities were predictive of post-operative pain.[142]

Socioeconomic class

In 2013 Clement et al., using the same cohort of patients that identified back pain as a predictor of outcome, reported that socioeconomic class was an important determinant of outcome,[146] with higher socioeconomic class associated with better outcome. This was consistent with a finding by Judge et al. in 2012.[22]

National Registry data

Baker at al has published studies using data from the HESS and the NJR. One, mentioned in the introduction to this chapter, used over 20,000 patients, and found that pre-operative PROM score, pre-operative general health rating, and the presence of anxiety and depression were the largest predictors of outcome.[95] In 2013, Baker at al again used national registry data to assess the value of pre-operative variables on satisfaction, finding that they were not as important in determining satisfaction as post-operative variables.[147] A caveat to this finding is the limited amount of data on psychological factors the NJR dataset produces.

The link between satisfaction and PROMs

Two papers of note have examined the link between the OKS and satisfaction. Judge et al. identified cut off for the absolute and change scores that splits patients into extremely high levels of satisfaction and high levels of satisfaction.[26] Kiran et al., from the same unit, suggested a method of using change scores corrected for baseline score – the Percentage of Potential Change Score (PoPC).[148] Although these papers are not directly linked to pre-operative prediction, they demonstrate that PROMs and satisfaction are intimately linked.

Radiographic severity

Greater radiographic severity has been linked to greater improvement over the course of a knee replacement.[149]

Predicting outcome

Various tools are currently available for the prediction of some outcomes for knee replacement. These were recently reviewed by Konopka et al.[150] Tools for predicting discharge to extended care facilities are available and their use has been reported to decrease length of stay (the Risk Assessment and Prediction Tool (RAPT) and the Predicting Location after Arthroplasty Nomogram (PLAN)).[150] Additionally, tools for predicting post-operative complications are available; however, their usefulness is limited as they require validation. Prediction models for length of stay in total and unicompartmental knee replacements have been produced by a centre in Singapore, although it accounts for less than a third of the variability and its external validity has been questioned. To date models attempting to predict functional and pain outcomes have been unsuccessful. This is largely due to the inability to account for enough variation in the outcome measure.

Case mix adjustment

In April 2015 case mix adjusted PROMs scores were used as part of the criteria for the Best Practice Tariff in knee replacements. The case mix methodology was based on a linear regression model developed from national datasets – these datasets represented information that is routinely collected as part of the national census, Hospital Episode Statistics (HES), and the NJR. Linking of this data gave the ability to generate a model based on over 30,000 observations. Explanatory variables included gender, age, ethnicity, self-reported disability, self-reported comorbidities, type of knee replacement, diagnosis, intervention, length of stay, patient demographics, co-morbidities, deprivation, type of operation, length of stay and whether assisted to complete the questionnaire. Therefore, the model was massively powerful to generate statistically significant results, even though the effects of individual explanatory variables may be small. Additionally, the model uses peri- and post-operative factors that would not be available to a pre-operative prediction model. This model is able to account for "around a quarter" of the variability in outcome.[40]

Analysis using a hold-out sample demonstrated that the model tends to over-predict for lower post-operative scores and under-predict for higher post-operative scores, but that as a predictor of mean post-operative scores it performed adequately with a high correlation observed between mean predicted and actual post-operative scores. However, it is debatable if case mix adjustment is a reasonable strategy when three quarters of the variability is unaccounted for. Determining how much variability needs to be achieved to make case mix adjustment worthwhile is a difficult task, and one that is not likely to reach unanimous consensus. This is especially true when the unknown variability could be a result of untested or unknown patient factors, as opposed to provider factors. Financial incentives/penalties when this is not known seems questionable.

Ongoing studies

There are various studies ongoing that are examining the prediction of outcome in knee replacements. The Arthroplasty Candidacy Help Tool (ACHE), run through the University of Oxford, is examining the prediction of outcomes in knee replacement.[151] ACHE aims to "develop a tool for GPs and/or hospitals to use to identify patients who are highly likely to benefit from hip or knee replacement surgery and guide those unlikely to benefit to other treatment options." This study is using existing databases to generate data, and therefore may not include some of the more recent psychological factors.

Another NIHR-funded grant, run through Southampton University, is aiming to use existing national and hospital databases to test established factors that affect outcome, and then derive a model based on these (the Clinical Outcomes in Arthroplasty Study; COASt).[152] A prospective arm, validating this model, will then be conducted and it due to complete in 2018.

The COmmunity based Rehabilitation after Knee Arthroplasty (CORKA), is a randomised controlled study examining different protocols for post-operative physiotherapy. This study uses a screening tool developed from the COASt study (as yet unpublished), to assess patients at high risk, and then randomises to different physiotherapy arms. It may be that different physiotherapy interventions are able to account for additional variability in outcome over and above pre-operative variables; however, this is of limited use for a prediction tool.

Funded by Arthritis Research U.K. the Targeted Rehabilitation to Improve Outcome after knee replacement (TRIO) study is examining the effect of targeted physiotherapy to patients who are functioning poorly in the early post-operative period.[153] Similar to the CORKA trial, this study is focussing on post-operative care as a variable in patient outcome.

To date, none of these trials have produced a prediction tool for patients with knee OA. Therefore, there is a need for a cohort study to examine the relationship between the explanatory variables identified in this chapter, and outcome. The next chapter describes the methodology for such a study.

Chapter 6. Development of a prognostic model for patients considering a total knee replacement

The previous chapter identified the factors that have been reported as important predictors of outcome after knee replacement. This chapter describes the methodology used in designing and carrying out the multicentre cohort study to develop a prognostic model for patients considering a knee replacement.

The development of such a model is the first step in the development of an outcome prediction tool, which would typically include external validation and impact assessment of the prognostic model. External validation and impact assessment does not form part of this thesis, although a discussion of future work from the development of the prognostic model is included.

6.1 Declarations

Aspects of this chapter have been published:

Barlow T, Dunbar M, Sprowson A, Parsons N, Griffin D. Development of an outcome prediction tool for patients considering a total knee replacement - the Knee Outcome Prediction Study (KOPS). BMC Musculoskeletal Disorders 2014, 15:451

Mrs P. Scott and the Arthritis Care Support Group (West Midlands) advised on the patient information material.

This study has been approved by the Northampton National Research Ethics Service (12/EM/0336), and all relevant local approvals at all participating sites.

6.2 Design

6.2.1 Introduction

I undertook a prospective multicentre cohort study including all six hospitals (NHS and private) that provide total knee replacements to the population of Coventry and Warwickshire. Six hundred patients were recruited, measuring potential predictors pre-operatively and outcome at six and 12 months post-operatively.

The work presented in this thesis concerns the development of a prognostic model to predict outcome in individual patients. This work is distinct from the protocol presented in the associated publication, which includes techniques involved in the development of an outcome prediction tool (e.g. internal validation). This work is ongoing within the KOPS team.

6.2.2 Pre-study work

Before conducting a cohort study examining patient factors, several issues require addressing. These include how best to measure certain factors (e.g. expectations), whether multiple questionnaires can be given simultaneously, and what outcome measures to use. Previous work, conducted by my supervisors, addressed these questions. The systematic review presented in Chapter 5 of this PhD thesis generated an up-to-date account of what was known regarding patient factors that were important in predicting outcome, and allowed the development of a strategy for measuring patient factors. An important point to note is that pain catastrophisation, a tendency to describe pain in an exaggerated way or ruminate over it, was not included, given the already significant patient burden, the lack of evidence at the time of their link to outcome, and the overlap between catastrophisation and other psychological measures used in our study (e.g. Anxiety, depression, helplessness).[154] However, since the development of the protocol, there is increasing evidence of the role of pain catastrophisation, as discussed in chapter 5.

With knowledge of the explanatory factors that were required, and how to measure them, it is possible to estimate how many patients were required in the cohort study.

6.2.3 Patient involvement

To refine the draft protocol I used UNTRAP (Universities/User Teaching and Research Action Partnership) to identify two members of the public that have had training in user involvement. One of the members was awaiting knee replacement surgery at the time. These members formed a collaboration with the research team in the refinement of the study protocol.

Subsequently, the study protocol and patient information sheets were presented and discussed with two local Arthritis Care support groups for further feedback. Revisions to the information sheets were made, and the feedback regarding the design, content, and importance of the study was exceedingly positive. During the research one members of the public was actively involved in the study steering committee.

6.3 Methods

6.3.1 Setting

Patients listed for a knee replacement within Coventry and Warwickshire (private and NHS hospitals) were screened for eligibility. The participating hospitals were: University Hospitals of Coventry and Warwickshire NHS Trust (UHCW); Hospital of St. Cross, Rugby (UHCW); Warwick Hospital (South Warwickshire Hospital NHS Trust); George Elliot Hospital (George Eliot Hospital NHS Trust; GEH); BMI Meriden Hospital, Coventry; and Nuffield Hospital Warwick, Leamington Spa.

6.3.2 Eligibility criteria

Inclusion criteria:

- A diagnosis of primary OA
- Managed with a primary total knee replacement during the study period
- Able to complete questionnaires and give informed consent
- Aged over 50 years

Exclusion Criteria:

- Unable or unwilling to give informed consent
- Unicompartmental knee replacement or revision procedure

6.3.3 Recruitment

At each participating centre the pre-operative pathway for patients was examined, and opportunities to "block book" the assessment of patients having knee replacements were identified. This process allowed each site to be visited once or twice a week to allow access to all patients on the waiting list for a knee replacement. For example, at Warwick Hospital patients requiring knee replacement were block booked into their pre-operative assessment on a Wednesday morning; at UHCW patients attending their pre-operative education class (which was a requirement to progress to surgery in the trust) were approached. The tailored approach required longer run in times in setting up, and was subject to variation in recruitment rates due to, for example, pre-operative patient pathways changing at an institutional level and patients being unable to attend certain days. However, it allowed flexibility at each site to adapt to changes over the course of the study, and it would have required a very large research team to achieve the recruitment targets without this approach. All patients were sent by post an invitation letter and a Patient Information Sheet before they attended the recruitment clinic.

Patients were recruited from their pre-operative clinic appointment where a baseline assessment of patient factors took place. Factors assessed were those identified in Chapter 5 as being important, and the method of measurement was either identical to the original studies, or, where no consensus on methods existed, questionnaires developed specifically for this purpose.[98]

The factors measured were:

- Age
- BMI
- Social support (measured by living alone)
- Deprivation (postcode, through the 2011 Census data)
- Knee status and knee pain (Oxford Knee Score - OKS)[17,112]
- General health (Short Form-36 - SF-36, which has eight domains across two subscales (mental and physical functioning)) [114]
- Medical co-morbidity (Co-morbidity questionnaire)[98]
- Joint co-morbidity (Joint Co-morbidity questionnaire)[98]
- Psychological co-morbidity (Hospital Anxiety and Depression Score)[155]
- Helplessness and coping style (Arthritis Helplessness Index)[154]
- Expectation (Knee Expectation Questionnaire)[98]
- Radiographic status (Ahlback Score – the Ahlback score was measured using templates as described by Dieppe).[156]

Patients were followed up at six and 12 months by postal questionnaire using the OKS, the SF-36, and several satisfaction scores. Satisfaction scores included a version of the satisfaction score developed and validated by Mahomed.[157]

Patients' general preference for a bottom line prediction of outcome (as described in Chapters 3 and 4) led to the addition of a question measuring decision regret. This question has been used in the literature previously, but has not been validated:[158,159]

"Knowing what you know now, would you still have the operation on your knee"

All questionnaires used in the study can be found in the appendix (section V).

6.3.4 Outcome Measures

The primary outcome measure was knee function as measured by the OKS at one year after operation.[112] This condition-specific measure is a 12-item Patient Reported Outcome Measure (PROM), specifically designed to measure knee pain and function. It has been well validated for this group of patients and is used by the Department of Health.[17]

The secondary outcome measures were the SF-36,[114] a 36-item patient reported measure of general health, which measures eight domains of health, including both physical and mental wellbeing. The two measures of satisfaction described above were also included.

The primary aim of this research was to develop a prognostic algorithm. Therefore, two private hospitals, as well as teaching and district general hospitals were included in the sample. It was therefore expected (and desirable) to have some differences in the inpatient management – this forms the basis of having a sample that is representative of the U.K. population as a whole, and is one of the main strengths of the study. The knee replacement procedure (inpatient stay, operation, and post-operative care) was treated as a single, common intervention. This approach is pragmatic, and it is likely that a proportion of the variance in patients' post-operative scores will be missed by intra- and post-operative factors. However, the aim was to develop a prognostic model applicable to many different settings. Additionally, previous reports have suggested that the proportion of the variance accounted for by intra- and post-operative care is small.[22]

6.3.5 Sample Size

I designed the study to have an 80% power to detect associations, at the 5% level, between pre-operative factors and outcome, with a correlation coefficient of 0.2. This will predict factors that account for more than 4% of the variation in the primary outcome measure (cohens effect size equal to 0.042), which is below the clinically detectable changes for the OKS, allowing for 10 explanatory variables included in the final model.[160] This requires analyse of 400 patients (calculation performed by Dr Parsons using the pwr package in the statistical software R,[161] which implements the methods of Cohen for a linear model).[162] This calculation is consistent with rule of thumb methods available for determination of sample size, that typically allow 10 patients per explanatory factor.

Our recruitment target was 600 patients. This allowed for a loss to follow up of 20% (although a loss of around 10-15% was expected in line with similar cohort studies), [89-92,122,163] and a further 80 patients to allow for unexpected events.

Feasibility work, used in the development of some of the questionnaires, demonstrated that 80% of eligible patients consent to participate.[98] The participating hospitals conduct around 1500 knee replacements each year. When planning the study I expected over 1000 patients would be eligible for inclusion in the study, and 800 would consent to participate over one year. The recruitment target of 600 patients was somewhat lower than this to allow for any unexpected recruitment problems. Although no serious problems in reaching this target were anticipated, the pilot study took place at one institution, and a potential drop in recruitment rate when extending the study over multiple sites was possible. Additionally, the amount of data to be completed by each patient was higher than in the development work – the volume of data requested was tested with our UNTRAP members and through a series of focus groups. It was thought to be acceptable; however, any more would have been "too much".

6.3.6 Data analysis

The primary analysis used multiple linear regression models to identify patient factors that were significantly associated with the OKS, the SF-36 (the primary and secondary outcome measures – both have been validated for this group of patients). Logistic regression models to assess dichotomous outcomes (satisfaction) are also used. Diagnostic analysis was used to assess model assumptions.

Model building

Before model building I decided that age, gender and OKS should be included as necessary parts of the model. This allows the model to be corrected for basic demographics and knee function of patients presenting for knee replacement. Complete case analysis, reflecting participants that had no missing data for any of the variables entered into the model (whether included or not), was used.

Forward stepwise analysis, using a p-value of 0.05 for inclusion and 0.1 for exclusion, was then used for explanatory variable selection using SPSS version 22.[164] Examination of each included variable using drop one diagnostics was performed. The Akaike Information Criterion (AIC), which is a measure of how well a model fits the observed data and includes a penalty for the complexity of the model, was included in the drop one diagnostics to aid explanatory variable selection.[165] The AIC was used to protect against over fitting the model, which is a risk with forward stepwise regression.[165]

Assumption testing

Formal testing for independence of observations is not considered necessary because it was assumed that each case (person) was independent of the next (no patient was included twice in the study). Linearity of associations between each explanatory variable and the dependent variable was assessed informally by scatterplots. Multicollinearity was assessed by entering all explanatory variables into a linear regression model in SPSS. This allowed the generation of Pearson's correlation coefficients between all variables. The assumption of homoscedasticity of residuals (indicating the variance of the residuals is the same for all values of predicted variable) and normality of residuals were tested on the fitted model. Homoscedasticity and normality of residuals were assessed informally using residual versus prediction scatterplots and QQ plots respectively.

A loss to follow up of 10-15% was expected and complete case analysis as the primary analysis was used. As a sensitivity analysis to explore the effects of missing data, multiple imputation using standardised methods available through SPSS version 22 (i.e. Multiple Imputation using Chained Equations) was used.[164] Results of both imputational analysis and complete case analysis are presented.

The statistical analysis allows weighting of the significant pre-operative factors, providing an estimation of outcome.

6.3.7 Assessment of recruitment strategy

Two approaches were used to demonstrate the representativeness of the study population. Firstly, baseline data on the knee replacements that were performed at each of the centres over the recruitment period was obtained. These data were generated from hospital coding data, and included the numbers of knee replacements, along with the age and gender of the patients. This allowed an estimation of the number of patients that were missed by the screening strategy, and a basic comparison of demographics between those groups. Secondly, comparison of the study population to basic demographic data from the National Joint Registry is presented.[17]

6.4 Reflection on the design of the cohort study

This section describes the justification for conducting a multicentre cohort study using patient factors to develop a prognostic algorithm in patients considering a knee replacement. If this algorithm is able to predict enough variability, it could be used to develop an outcome prediction tool that supports patients' decision-making, hence improving quality of care. It would also facilitate interpretation of evidence from published observational studies of different interventions by determining whether groups of patients were similar, and allow *post hoc* adjustment of clinical effectiveness studies for risk profile. The ability to adjust samples for case mix is particularly topical in view of the Best Practice Tariff for knee replacements, and the publication of individual surgeon data.

The main strength of this study is the breadth and comprehensiveness of the patient factors selected for inclusion in the model-building process; many of these factors have previously been shown to correlate with important outcomes after surgery. Another strength is the size and demographic of the patient population sampled, which includes both NHS and private patients. Although this represents a relatively small geographical area, that area lies in a region with diverse ethnicities and deprivation indices, and should provide adequate coverage of the spread of data required to develop a prognostic model.

However several limitations of this approach exist. Selection bias may be present depending on the personality of patients who are more likely to agree to take part. Feasibility work (not part of this thesis) suggested that around 80% of patients who are eligible to take part consent to do so. Examination of the basic demographics of patients who refuse allowed comparison between this group and the study population.

An additional factor that could have influenced selection bias is missing patients that may have been eligible. Our approach to this issue has been the development of protocols to identify eligible patients at each site. This process was tested by comparing those screened against those not screened by using hospital coding data. This approach has several caveats. Given the large populations involved (approximately 1000 patients screened, and 500 not screened), statistical tests between groups are powerful, and are capable of showing statistical significance for small, potentially meaningless, differences. For example, a t-test for a sample size this large comparing ages is likely to be able to detect a difference smaller than one year. All ages were rounded down, and therefore the power of the study at least equals the error in the recording of data. Additionally, the reliability of the coding data is questionable. Previous studies have demonstrated errors in coding data of between 1.1 and 45.8%, with an average of around 7%.[166]

It may not be possible to predict enough variability in outcome to produce a clinically useful tool. As our model is based on a systematic review that identified known prognostic factors and has included all of them, it is highly likely to explain more of the variability. However, the variability that each factor can account for will not be simply additive.

Recently identified factors, for example pain catastrophising, have not been included in our model.[141,142] The presence of pain catastrophising does have an important bearing on outcome, but it is not only its presence, but also how it influences a patient's behaviour and ability to cope. This score was not included in the original protocol, as it was unclear how strong the association was at the time of development. However, it is likely that some (if not all) of the variability this factor predicts will be captured by the HADS, Arthritis Helplessness Index (which includes the dimensions of internality and helplessness – closely correlated with catastrophisation) and several dimensions of the SF-36 (vitality, bodily pain, emotional role functioning, social role functioning, mental health).[154]

The OKS may not have enough discriminatory power in high functioning individuals (ceiling effect). However, it is good at discriminating between moderate and poor functioning individuals (the groups that are of more interest). Additionally, measures of satisfaction are being used. Although satisfaction is not as robust a measure of outcome as the OKS, it provides a "bottom line" prediction that patients generally prefer (as discussed in chapters 3 and 4).

Chapter 7 – Results and discussion of multicentre cohort study

This chapter reviews the screening and recruitment process, with a view to describing and testing for possible selection bias. Patient retention, baseline characteristics, and missing data are described. Multiple imputation is used as a sensitivity analysis to explore patterns of missingness.

A multiple linear regression model is described for predicting six month OKS and 12 month OKS, SF-36, and satisfaction. Logistic regression is used to generate a prediction model for decision regret. The properties of the models are described and their usefulness for predicting outcome is explored.

7.1 Declarations

Patient recruitment was assisted by the Research Associates of Warwick Orthopaedics (approximately 20%). Database set up was conducted in collaboration with Warwick Orthopaedic staff. Follow up of patients was assisted by Warwick Orthopaedic staff (75%). Data input was conducted by Warwick Orthopaedic staff. Dr I Ahmed, Dr D Bhatt, Mr B Mishra assisted in grading of pre-operative radiographs. Mr J Skliros designed the layout of the questionnaire packs. Calculation of domain scores for SF-36 was conducted by Dr N Parsons.

7.2 Results

7.2.1 Patient screening and recruitment

Nine hundred and ninety-nine patients were screened for inclusion into the study from March 2013 to July 2014. Six hundred patients were recruited into the study. Table 10 shows the reasons for patients not being included in the study.

Of note, 65 patients were screened that were not listed for a total knee replacement, but other, related operations (e.g. unicompartmental knee replacement). Twenty patients, who were initially recruited to the study, were removed. These patients did not have an operation, could not adhere to the study protocols (not return questionnaires), or had an operation other than a total knee replacement (unicompartmental knee replacement). For the majority of patients (approximately 80%) I assessed capacity at the time of recruitment. This assessment was performed by the Research Associates for the remainder of the patients. Only three patients were thought to lack the capacity to complete the questionnaires.

Table 10: Numbers of Patients Screened

	UHCW*	Rugby*	Warwick*	George Elliot*	Nuffield*	BMI*	Total
Lacks Capacity	2 (0.6%)	0	0	1 (0.9%)	0	0	3 (0.3%)
Not OA	7 (2.2%)	2 (0.7%)	0	0	0	0	9 (0.9%)
Poor English	6 (1.9%)	1 (0.4%)	8 (3.6%)	4 (3.4%)	0	2 (5.6%)	21 (2.1%)
Unable to complete	5 (1.6%)	3 (1.0%)	3 (1.4%)	2 (1.7%)	0	0	13 (1.3%)
Not total knee replacement	24 (7.5%)	33 (11.7%)	3 (1.4%)	4 (3.4%)	0	1 (2.8%)	65 (6.5%)
Too young	8 (2.5%)	9 (3.2%)	5 (2.3%)	3 (2.6%)	3 (13.0%)	0	28 (2.9%)
Previously recruited	0	1 (0.4%)	4 (1.8%)	1 (0.9%)	0	1 (2.8%)	7 (0.7%)
Refused	91 (28.2%)	71 (25.2%)	37 (16.8%)	23 (19.8%)	6 (26.1%)	5 (13.9%)	233 (23.4%)
Removed from study	9 (2.8%)	5 (1.8%)	2 (0.9%)	4 (3.4%)	0	0	20 (2%)
Recruited	170 (52.8%)	157 (55.7%)	158 (71.8%)	74 (63.8%)	14 (60.9%)	27 (75.0%)	600 (60%)
Total number screened	322 (100%)	282 (100%)	220 (100%)	116 (100%)	23 (2.3%)	36 (100%)	999 (100%)

**Percentages by individual hospital site*

Process of screening and recruitment

By site

At all sites a recruitment process was set up: this generally took several weeks, and inevitably resulted in some patients being missed to recruitment. The process followed at each hospital was:

UHCW and Rugby St Cross

Patients were recruited from their pre-operative education class. This class is a compulsory part of their pre-operative pathway. Research Associates predominantly recruited patients at UHCW, and I recruited all patients at St Cross.

Warwick, Nuffield and the BMI

Patients were recruited from their pre-operative assessment. This is a compulsory part of their pre-operative pathway. Patients were block-booked into one pre-operative clinic, where I was present. This process led to patients being missed due to requesting other dates, capacity issues in the designated recruitment clinic necessitating patients attend on alternative days, and administrative errors (especially during the set-up of clinics).

GEH

In GEH the original pathway involved patients who were listed for a knee operation being given a date for their pre-operative assessment. The study originally targeted these clinics for assessment, with patients listed for knee replacement being block booked into clinics.

However, due to a hospital wide alteration in the pathway for pre-operative patients, an alternative approach was needed from September 2013 onwards. Patients who were listed were offered an appointment straight away with the pre-operative nurses for pre-operative assessment. This change was initiated to decrease the number of visits for patients, in an attempt to create a "one stop shop". Providing the manpower to recruit patients at every clinic referring patients for a knee replacement was not feasible.

As a compromise, I targeted patients at their pre-operative knee physiotherapy group. This group had a significant non-attendance rate. To address this I arranged with the orthopaedic department, in collaboration with the Clinical Director for Surgery, to highlight to all patients that this formed a compulsory part of their care. This did not completely remove the non-attendance at the pre-operative clinic appointments. Overall, 51 patients did not attend (DNA) that would have been appropriate to take part in the study (44%); however, for the study overall, DNA patients made up only 5.8% of the screened population.

Recruitment Rate

Table 11 shows the number of patients recruited from each site, with Figure 8 providing a line graph for the cumulative number of patients recruited by site.

Table 11: Numbers recruited by site

Month	UHCW	Warwick	Rugby	GEH	Nuffield	BMI	Total
March 2013	1	0	0	0	0	0	**1**
April 2013	12	0	0	0	0	0	**12**
May 2013	6	14	0	0	0	0	**20**
June 2013	14	14	3	0	0	0	**31**
July 2013	11	10	15	8	0	0	**44**
August 2013	9	18	2	4	0	0	**33**
September 2013	4	7	9	0	1	0	**9**
October 2013	7	13	15	8	2	3	**59**
November 2013	13	5	15	6	1	0	**37**
December 2013	10	4	10	5	2	1	**35**
January 2014	12	18	13	17	2	1	**63**
February 2014	10	11	11	5	1	6	**44**
March 2014	15	10	11	6	2	2	**46**
April 2014	27	6	11	8	2	2	**56**
May 2014	2	18	24	4	1	10	**60**
June 2014	13	8	7	2	0	2	**30**
July 2014	5	3	11	1	0	0	**20**

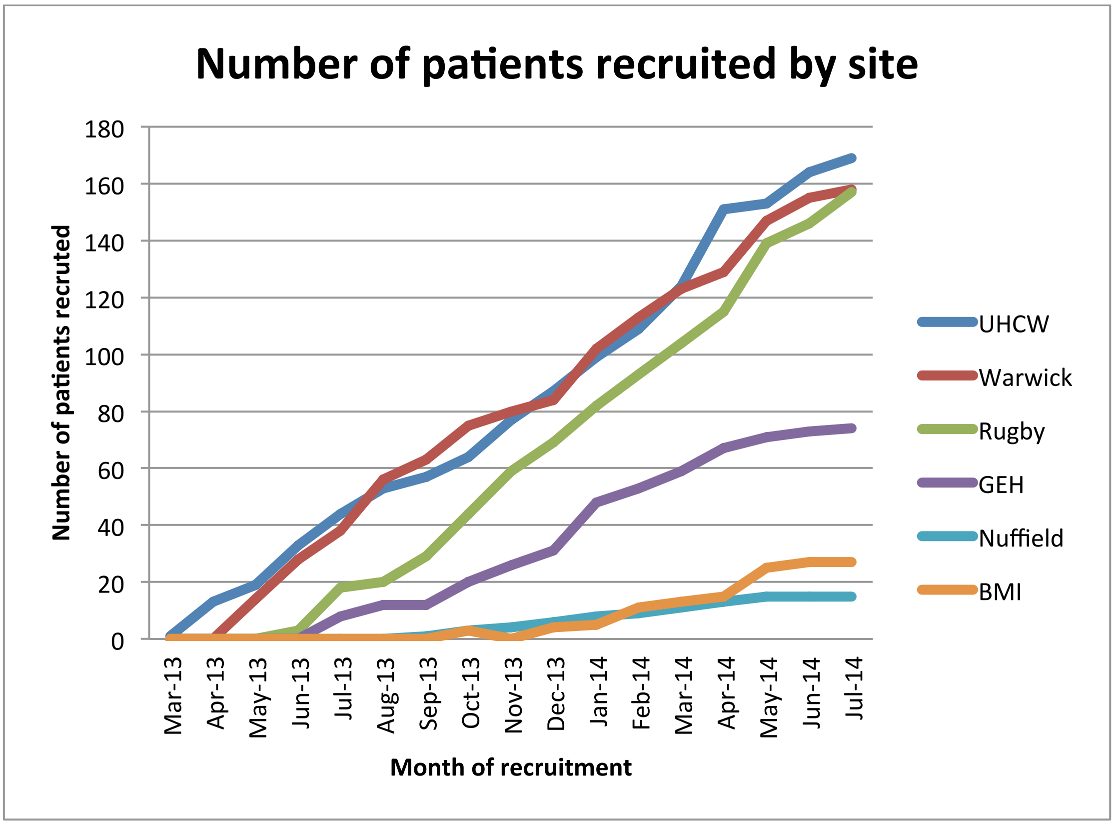


Figure 8: Recruitment rate by site

Variations in recruitment rate

There was a drop in recruitment in July 2013 at Rugby St Cross Hospital. This coincided with annual leave.

A large drop in recruitment was seen in August and September 2013 across all sites. Discussion with members of staff at all sites revealed that this was a yearly occurrence due to the amount of annual leave taken by staff over this period. This resulted in less patients being listed for orthopaedic procedures (due to less orthopaedic clinics being run) and less patients going though pre-operative clinics due to decreased staff numbers. These factors are thought to be responsible for another, smaller drop in recruitment in December 2013.

The third drop is seen in June and July 2014, at the very end of recruitment. This was due to two factors. Firstly, at both private hospitals (BMI and the Nuffield) the pathway for patients attending pre-operative clinics was altered (these changes happened simultaneously, but independently of each other). This required the re-arrangement of the recruitment strategy for the study. On the basis that few patients were required to fulfil the study's target, recruitment was shut down. Secondly, Research Associates were relied upon for recruitment at one site (UHCW). Due to difficulties with staffing, clinics over a three-month period (May to July) were intermittently staffed.

Deficiencies in the screening process

By examining the process of screening and recruitment, and the reasons that some patients were not approached to enter the study, some assertions can be made on the presence of selection (sampling) bias. Although representativeness is not a requirement of building a prognostic model (the requirement is rather ensuring that a full spread of data is available for analysis in the model), a representative sample of 600 patients is likely to give a sufficient spread of data.

Patients that were not screened, but are likely to be no different to the study population

Patients who were not screened, but are likely to be no different to the study population, include those patients that

- Were not screened due to staffing issues (e.g. annual leave) that resulted in designated pre-operative clinics not being staffed.
- Were not screened due to capacity issues within designated pre-operative clinics
- Were booked into alternative clinics due to administrative errors
- Requested alternative pre-operative clinic dates within the normal working week

Due to the processes that resulted in their not being screened, it is unlikely that they were significantly different to the screened population.

Patients that were not screened, but could be different to the study population

There are two groups that were not screened that could represent sub-populations that are different to the study population:

- Patients who Did Not Attend (DNA) their appointments
- Patients who altered their pre-operative appointment to a weekend

Patients who do not attend appointments may do so for various reasons (e.g. work commitments, childcare commitments, limited mobility). With this study, a psychological difference between patients who do attend and who do not attend has a logical consistency, and informed the original development of the local protocols at each site. Also, patients who do attend may have different expectations compared to those who do not.

Table 12 gives the rates of DNA at each site. One site (GEH) had a large number of DNA appointments (30.5% of total patients screened); however, DNAs made up less than 4% at each other site, and only 5.8% of the total study population.

Table 12: Did not attend (DNA) rates by site

	UHCW	Rugby	Warwick	George Elliot	Nuffield	BMI	Total
Did Not Attend	0	9 (3.1%)	0	51 (30.5%)	0	1 (2.7%)	61 (5.8%)

Demographic analysis of patients who DNA against those who did attend was undertaken for GEH. Analysis of the study as a whole was not undertaken. Due to the disproportionate amount of DNA at GEH, comparing the DNA population to the study population as a whole is similar to comparing the population of GEH to the study as a whole. The baseline demographics demonstrate that GEH patients are, on average, three years younger. Therefore there is likely to be a difference based on the different proportions of patients from each hospital site, rather than any difference between patients that DNA and those that did not. Table 13 gives the mean ages and standard deviations for each group from GEH. There was no significant difference using a t-test. Also, a chi-squared test was not significant (p=0.994) for a difference between groups with regards to gender.

Table 13: Age of those who attended and DNA for GEH

	Group	N	Mean	Std. Deviation	Std. Error Mean	Significance
Age	DNA	49	66.5	9.2	1.3	0.202
	Not DNA	95	68.5	8.8	0.9	

Patients who altered their pre-operative appointment to a weekend are the second group that may cause selection bias. For several months in 2015 (April to July) there were pre-operative appointments occurring at the weekend at one site (UHCW). This process was in place to cover a backlog of patients that had developed due to a lack of throughput in the pre-operative assessment process. It is reasonable to assume that the subpopulation of patients that requested weekend pre-operative appointments were different (for example they could be a younger, working population). There was no selection process in place for weekend lists, so there is no reason to believe that patients on these lists were significantly different, unless they had specifically requested a weekend.

The total number of patients that went through the weekend lists was small (roughly 100 in total). Additionally, this is also the time that staffing issues among the research associates were at their height, and this will have diluted the effect of this subpopulation of patients. This means that the overall effect on the demographics of the study sample is likely to be minimal. To test this an exploration of differences by age and gender of patients who where not identified during the screening process is provided in the next section.

Assessment of patients missed by the screening process

The aim of this study is to develop a prognostic algorithm, and therefore patients with a wide range of factors should be included in the model building phase. A representative sample will give confidence that a wide cross-section of the population of interest has been included: this does not mean that the sample has to be truly representative of the general population having knee replacements, but is does have to represent that cross section. Therefore, the representativeness of the study sample was explored.

Baseline data on the knee replacements that were performed in each of the sites over the recruitment period was obtained. This data was generated from hospital coding data, and included the numbers of knee replacements, along with the age and gender of the patients. This allows an estimation of the number of patients that were missed by the screening strategy, and a basic comparison of demographics between those groups.

This approach has several caveats. Given the large baseline population the statistical tests are powerful, and may reveal statistically significant differences that are smaller than the measurement error (e.g. differences of smaller than one year). Therefore any statistical differences need to be treated with caution.

Also, the reliability of hospital coding data is questionable. Previous studies have demonstrated errors in hospital coding data of between 1.1 and 45.8%, with an average of around 7%.[166] The data collected was relatively straightforward, so it is reasonable to expect it to fall on the lower end of this range. However, compounding this error rate, there are additional issues with the hospital coding data within our study. For example, some hospital sites were unable to provide coding data for patients that only had knee OA (and therefore the coding data included patients with other types of arthritis). Given the prevalence of each condition this is unlikely to alter the results to a large extent, but could account for inflation in the numbers of patients in the coding data by around 5%, and could alter the population demographics.

Additionally, at UHCW and Rugby, the time from pre-operative appointment to operation could be up to 12 months. This resulted in difficulties in calculating the timeframe that patients would have been eligible during the recruitment period – this was resolved by using Korner weeks (the length of time from referral to operation) to correct for the time delay. This has problems in itself as the referral and the time of recruitment were not identical (although closer than the time of recruitment and actual operation data). This likely increases the number of patients included in the coding data (particularly when theatre throughput is the limiting factor, as was the case at UHCW and Rugby St Cross). This approach also introduces a further source of error by using additional datasets within the coding framework, and inevitably led to several weeks at the beginning and the end of the recruitment period that were highly unlikely to include patients that were eligible, but had to be included in the coding data so as not to miss any recruited patients. Again this would increase the number of patients in the coding data.

Combined, there are three factors that are likely to cause an overestimate of the number of people "missed" by the recruitment strategy. The result of this is a highly conservative estimate of the success of the recruitment strategy. Additionally this could alter the demographics of the population of patients that were not screened that, when combined with high (but unknown) error rates in the coding data, make any statistical inference of difference prone to error.

Despite these weaknesses an assessment of age and gender for all patients who would have been eligible for the study at each site was conducted by examining the hospital coding records at each site. This allowed comparison of those who were screened against those who were not.

Overall 715 patients were identified in hospital coding that were not screened. Their mean age was 70 years (sd 8.9) and 31% were male. This was compared to the population of patients that were screened, excluding those that were unlikely to appear in hospital coding (e.g. not a total knee replacement, or too young). This group consisted of 848 patients with a mean age of 70 years (sd 8.9) and 42% male. Ages were not significantly different (p= 0.595; independent samples t-test), whereas gender was (p<0.001; chi-squared test).

The significant result is subject to the limitation described above; however, given the difference in genders between those screened and those not screened, comparison of those screened with the population of patient having knee replacement in England and Wales was undertaken using information from the National Joint Registry (2013). Using this data, the median age of someone undergoing a knee replacement is 70 years, with 58% being female (42% male). This compares favourable with our study (mean age 70 years, 44% male), and our screened population (mean age 70 years, 42% male) (Table 14). This provides strong external evidence that our processes to screen patients to this study were sound and likely to provide high quality, reliable and representative data.

Table 14: Age and gender of different populations

Population	Mean age	Percentage male
National joint registry	70	42%
Coding data from included hospitals	70	31%
Patients screened	70	42%
Patients in study	70	44%

Deficiencies in the recruitment process

Seventy-two per cent of eligible patients consented to take part, with 28% refusing. Patients who refused to participate are a key group, as it is reasonable to think that these patients could be different from the rest of the study population. Data on the reasons for refusal were not compulsory for patients to complete and was not routinely collected. However, the most common reason cited to the study team was the time it would take to complete the study paperwork.

To examine if this group was different to the study population, age and gender were compared. Table 15 demonstrates a significant difference between populations as regards age (p<0.001; t-test), with those who refused tending to be older. The difference in mean age is approximately three years. Although this difference is significant, it is unlikely to be important. A difference of three years is small, and the study included patients from 50 years to 91 years.

Table 15: Comparison of age of those recruited and those who refused

	Group	N	Mean	Std. Deviation	Std. Error Mean	Significance
Age	Recruited	600	69.0	8.75	0.36	<0.001
	Refused	228	72.1	9.06	0.60	

Gender proportions were similar across groups with no significant difference between patients who refused or those who accepted entry to the trial (p=0.370; chi-squared test).

7.2.2 Patient retention

Figure 9 shows the number of patients at each stage of the study. Six hundred patients were recruited into the study. Overall 83 patients were excluded from the study: Operation cancelled (17); not a total knee replacement (2); incomplete or missing data (7); died (3); protocol breach (too young at time of operation - 2); withdrew (1); and over six months between recruitment and operation (40). The team agreed that patients who waited over six months between recruitment and operation should be excluded to safeguard against baseline measurements changing by the time of operation.

A further 11 patients with significant complications (Fracture (n=3), revision (excluding revision for pain) (n=5), patella tendon rupture (n=1), significant medical co-morbidity (e.g. dense stroke) (n=2)) were excluded from analysis. Significant complications were excluded because our aim was to produce an outcome prediction model. Complications were not going to form part of that model, and the rate of complications is well established for knee replacements. Therefore, an outcome prediction model excluding complications could be used for all patients with the normal pre-operative counselling regarding the risk of complication.

After exclusions, 517 patients were eligible for follow up at six months. A further patient was excluded at 12 months following a stroke.

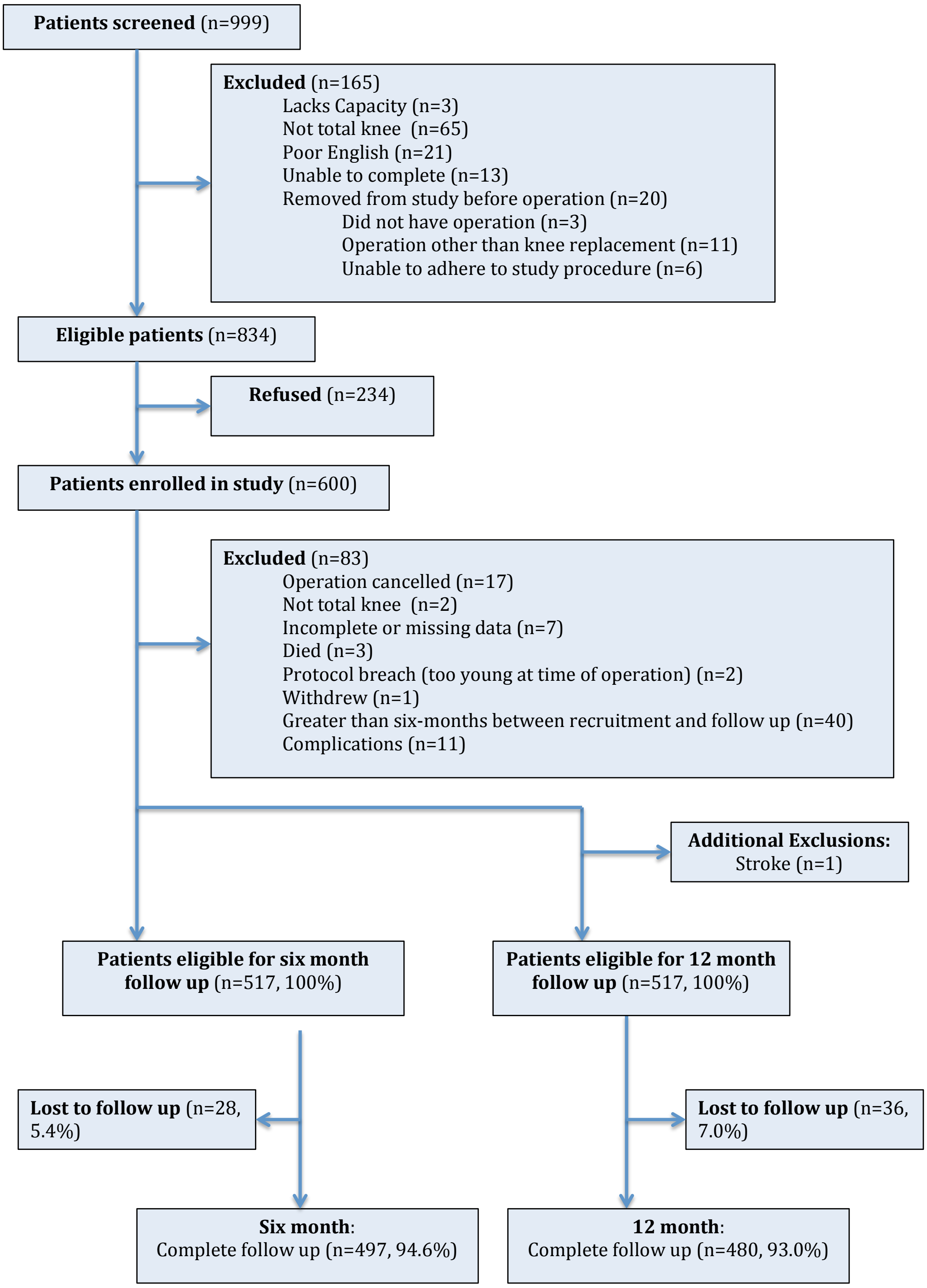


Figure 9: Flow diagram of patients included in KOP Study

7.2.3 Baseline patient demographics

The mean age of participants was 70 years (sd=8.8) and 56% were female.

Patients waited a median of 27 days (range 1-182 days) between measurement of baseline characteristics and operation.

Table 16 demonstrates means and standard deviations for all explanatory scale variables assumed to be approximately normally distributed, and Table 17 shows means and interquartile ranges for other explanatory scale variables. Boxplots of all scale variables are presented in Figure 11 to Figure 23.

Proportions for all categorical explanatory variables are displayed in Table 18. Severity of arthritis was assessed using the Ahlback grade (grades 1-5) which was then dichotomised into severe (grades 3-5) and not severe (grades 1-2) as per the methods used by Riis et al.[149]

Table 16: Explanatory scale variables (assumed approximately normally distributed)

Variable	Mean	Std. Deviation	N
Age	68.7	8.6	517
OKS Baseline	19.7	8.1	502
Body Mass Index (BMI)	30.5	5.7	457
Helplessness	12.4	2.7	485
Internality	14.1	2.7	485
Co-morbidity (number of conditions)	3.2	1.6	487
Physical Capacity Score (PCS)	21.3	9.0	466
Mental Capacity Score (MCS)	52.5	12.3	466

BMI is weight (kg)/height (m)^2; OKS, Oxford Knee Score, measured from 0 (poor function) to 48 (high function); Helplessness, measured from 5 (low helplessness) to 20 (high helplessness), Internality, measured from 6 (low internality) to 24 (high internality); PCS, SF-36 physical domain, measured from 0 to 100; and MCS, SF-36 psychological domain, measured from 0 to 100.

Table 17: Explanatory scale variables (assumed to be non-normally distributed)

Variable	Median	Interquartile range	Number
Deprivation Score	12.5	6.3 - 18.7	517
Expectation Score	43	39.5 - 46.5	488
Anxiety Score	5	2.4 - 7.6	488
Depression Score	3	1 - 5	490
Joint co-morbidity	3	1.5 - 4.5	451

Deprivation score, from the Index of Multiple Deprivation (UK Census); Expectation Score, from 0 (low) to 48 (high); Anxiety Score, Hospital Anxiety and Depression (HAD) sub-score, from 0 (low) to 20 (high), Depression score, HADs sub-score, from 0 (low) to 20 (high), joint co-morbidity used count of number of joints with pain in last week.

Table 18: Explanatory binary variables

Variable		Number (Percentage)
Gender	Male	214 (41%)
	Female	303 (59%)
Severe Arthritis	No	239 (48%)
	Yes	262 (52%)
Live alone	No	363 (76%)
	Yes	118 (24%)
Previous arthroscopy	No	319 (71%)
	Yes	133 (29%)
Lower back pain	No	247 (55%)
	Yes	204 (45%)

A key for Figure 11 to Figure 23 is available below (Figure 10). Boxes show interquartile range (25-75% extent of data) and bar is median (50% point). Whiskers (bars) are 1.5 times IQR. Outliers are defined by:

o = Outlier (value is less than or equal to the first quartile minus 1.5 times the interquartile range, or is greater than or equal to the third quartile plus 1.5 times the interquartile range)

* = Outlier (value less than or equal to the first quartile minus 3 times the interquartile range or greater than the third quartile plus 3 times the interquartile range)

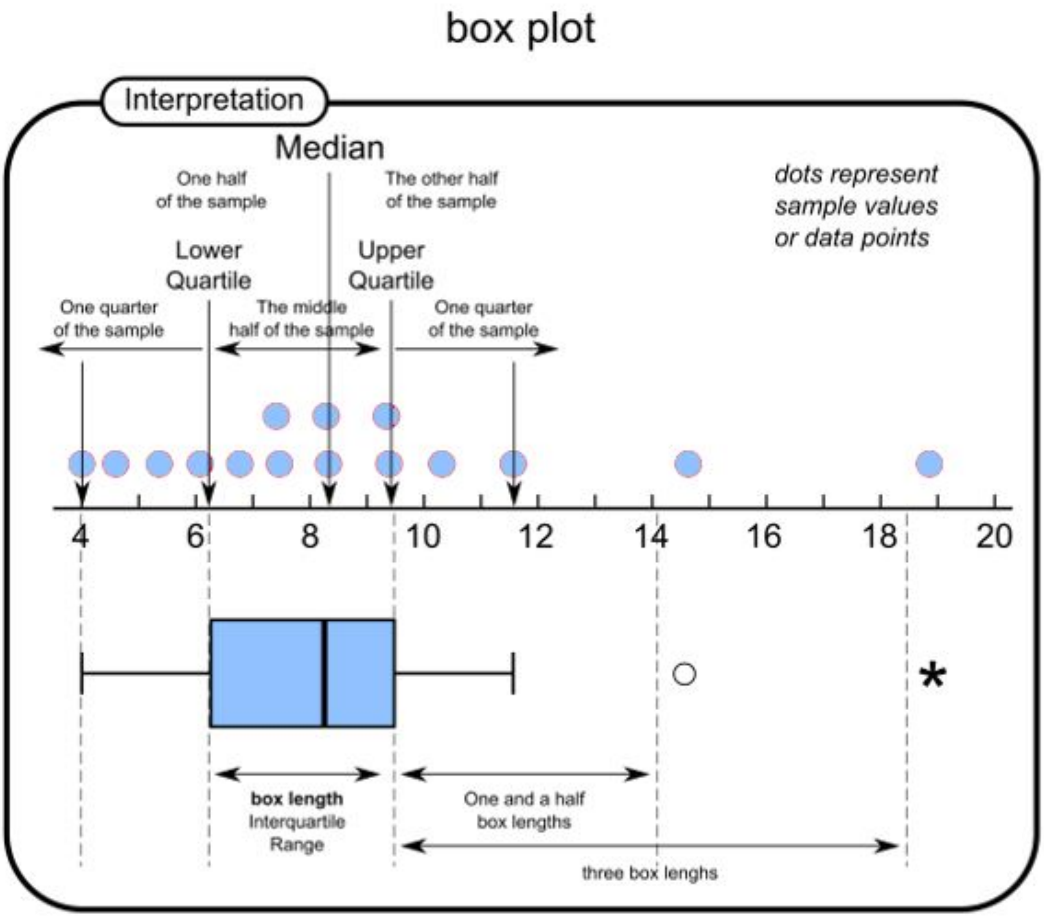


Figure 10: Key to boxplots

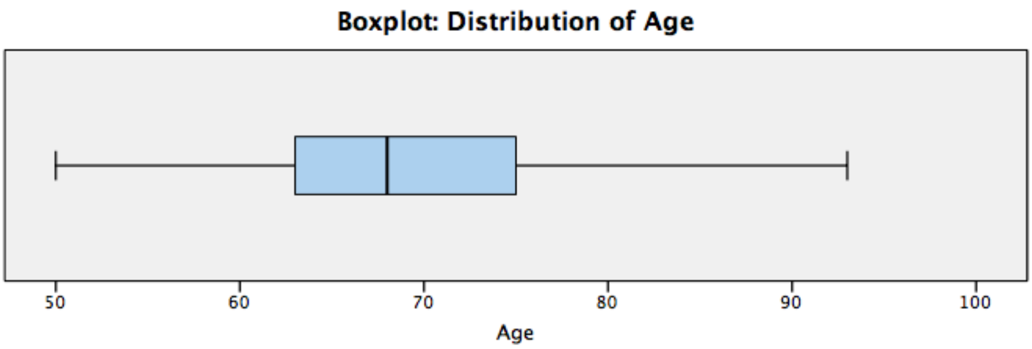


Figure 11: Distribution of age (range 50 to 92)

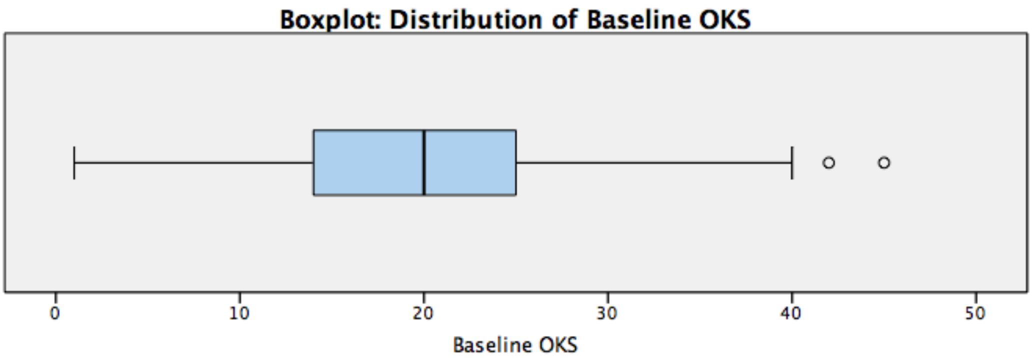


Figure 12: Distribution of baseline OKS. Range of possible scores 0 to 48 (higher score reflects better function)

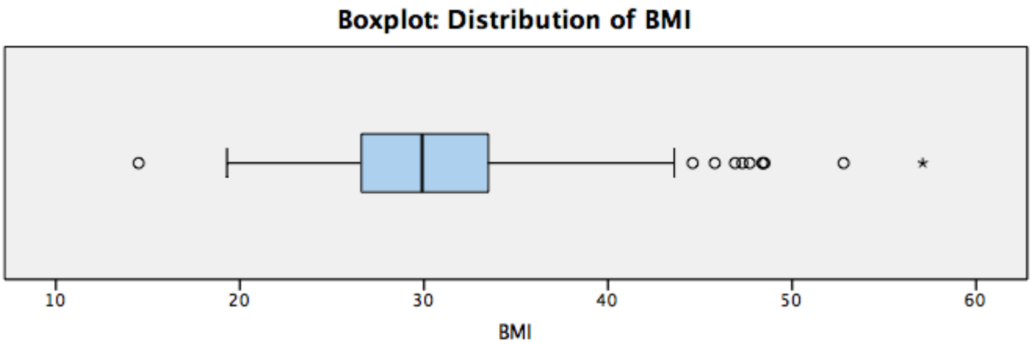


Figure 13: Distribution of BMI. Range of BMI 14.5 to 57.1.

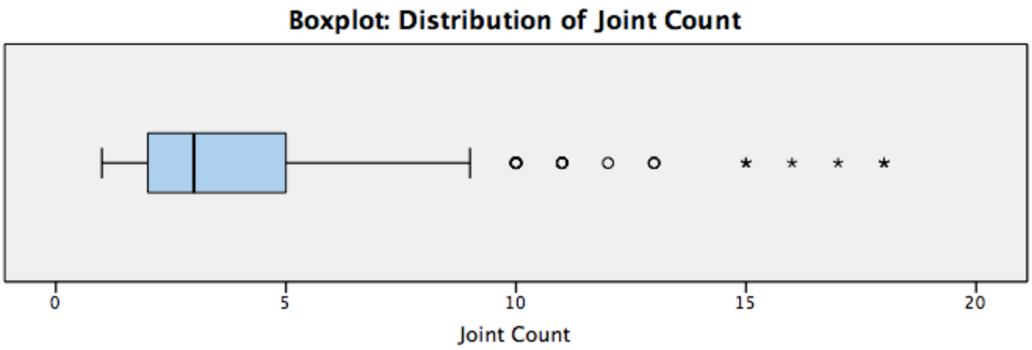


Figure 14: Distribution of joint count. Range of joint count 1 to 18.

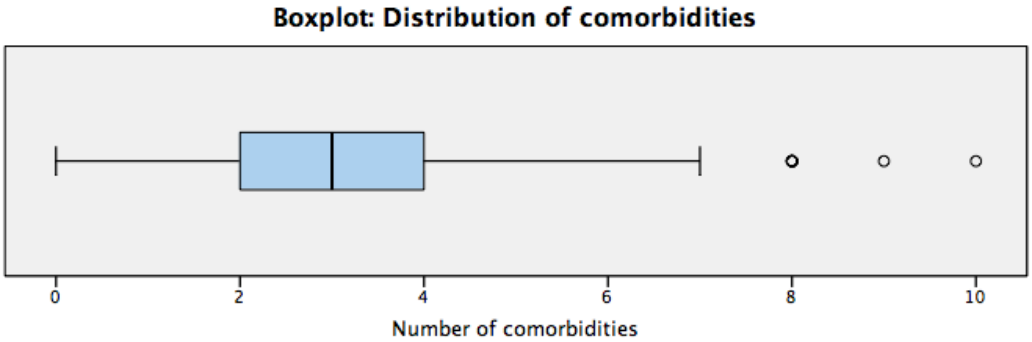


Figure 15: Distribution of comorbidities. Range of comorbidities 0 to 10.

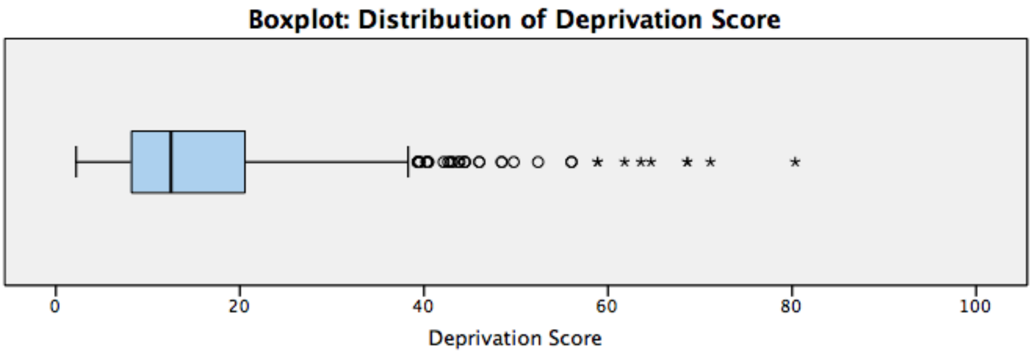


Figure 16: Distribution of deprivation score. Range of possible deprivation scores 0 to 100. Lower scores reflect less deprivation.

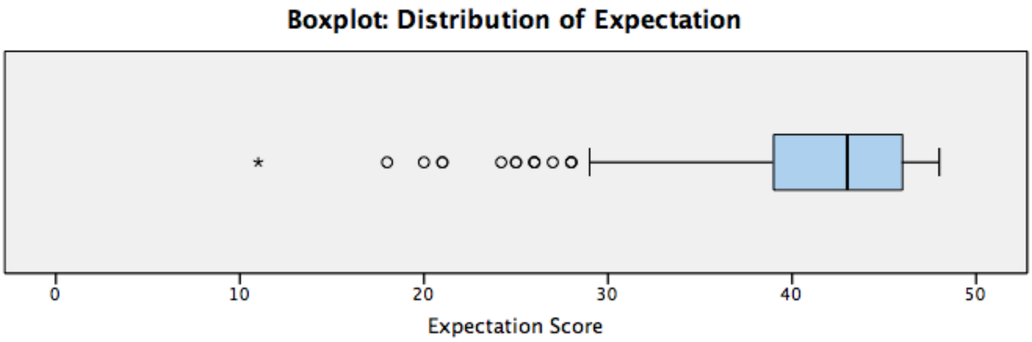


Figure 17: Distribution of expectation scores. Range of possible scores from 0 to 48. Higher scores reflect higher expectations.

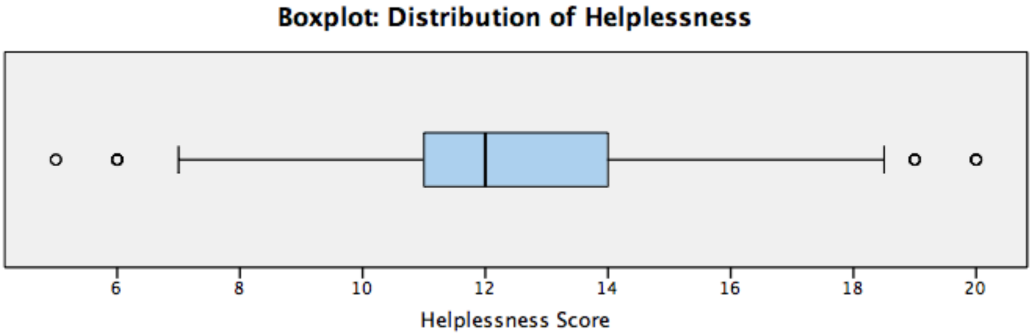


Figure 18: Distribution of helplessness scores. Range of possible scores 5 to 30. Higher scores reflect greater helplessness.

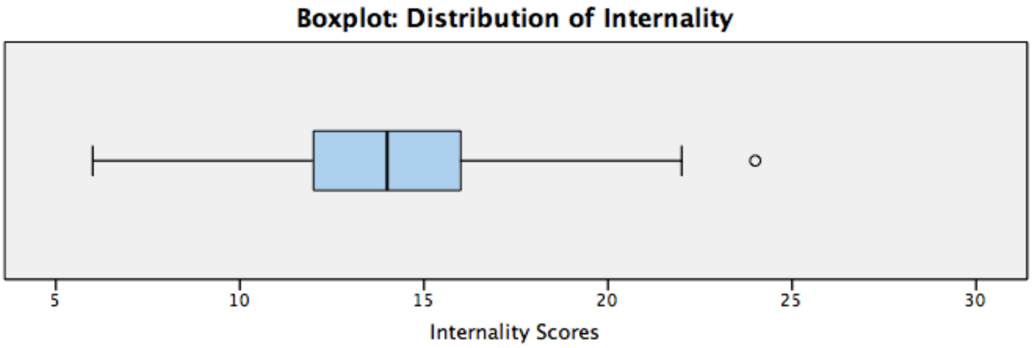


Figure 19: Distribution of internality scores. Range of possible scores from 5 to 30. Higher scores reflect more internality.

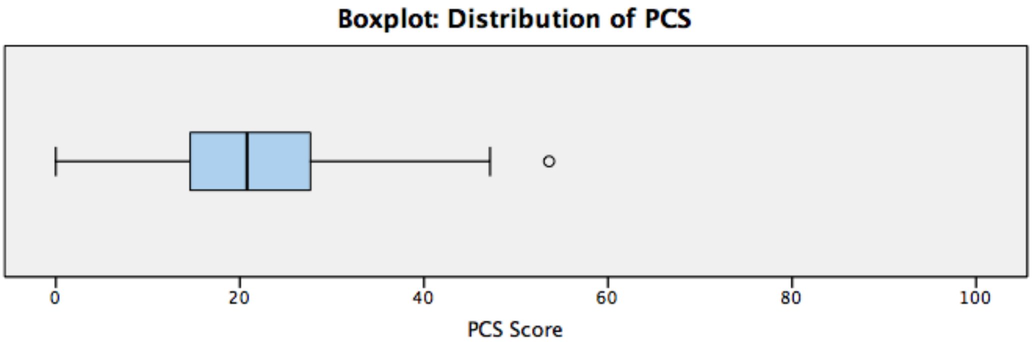


Figure 20: Distribution of PCS Scores. Range of possible scores from 0 to 100. Higher scores reflect better function.

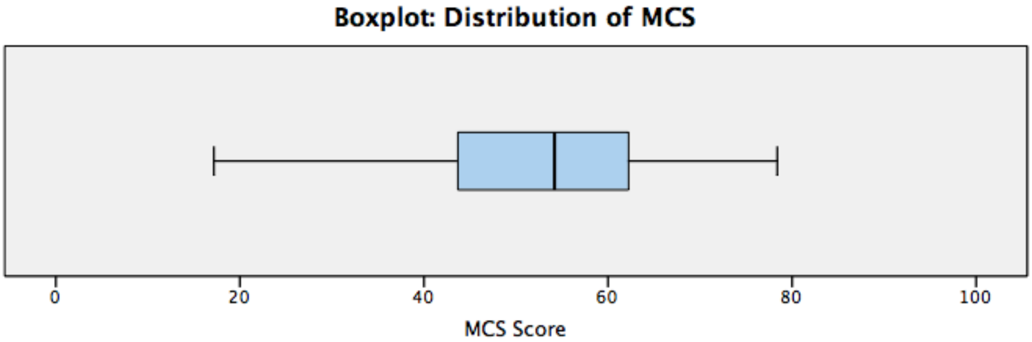


Figure 21: Distribution of MCS scores. Range of possible scores from 0 to 100. Higher scores reflect better mental health.

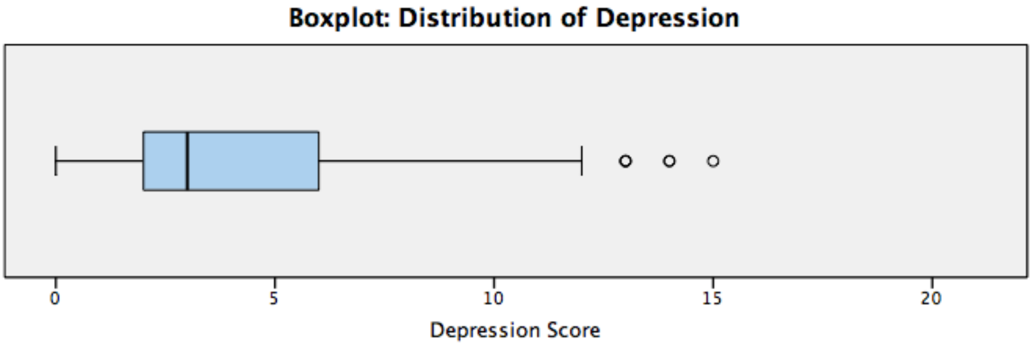


Figure 22: Distribution of depression scores. Range of possible scores from 0 to 21. Higher scores reflect more depressive symptoms.

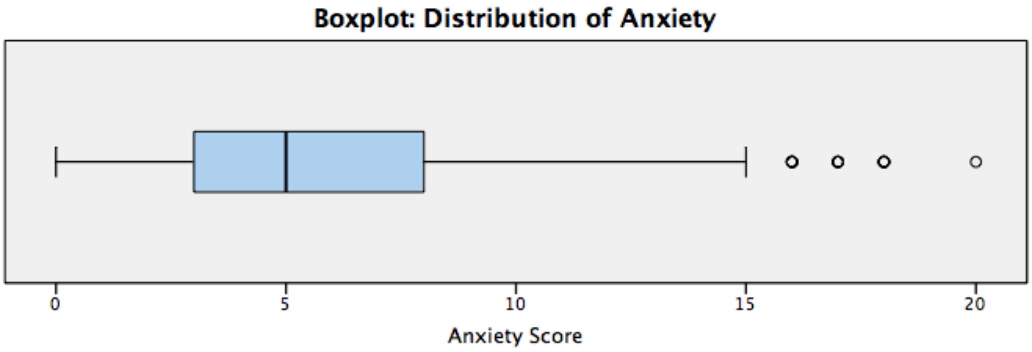


Figure 23: Distribution of anxiety scores. Range of possible scores from 0 to 21. Higher scores reflect higher anxiety.

7.2.4 Missing data

Missing data were present in 6.5% of values for all explanatory variables tested in the model. Complete cases were found in 284 cases (55%). Table 19 demonstrates the number of cases with missing data broken down by explanatory variable.

Table 19: Missing data in explanatory variables

Variable	N	Missing (Count)	Missing (Per cent)
Age	517	0	0%
Gender	517	0	0%
OKS Baseline	502	15	2.9%
BMI	457	60	11.6%
Severe Arthritis	501	16	3.1%
Joint count	451	66	12.8%
Back Pain	451	66	12.8%
Comorbidities	487	30	5.8%
Live Alone	481	36	7%
Deprivation Score	517	0	0%
Previous Arthroscopy	452	65	12.6%
Expectation	488	29	5.6%
Helplessness	485	32	6.2%
Internality	485	32	6.2%
PCS	466	51	9.9%
MCS	466	51	9.9%
Depression	488	29	5.6%
Anxiety	490	27	5.2%

Item-missingness in scores

For variables that consisted of scores, item-missingness was examined: item-missingness refers to the individual items that make up the composite score. Two patterns emerged with the baseline OKS and the expectation questionnaires. With the OKS questionnaire five patients missed the first five questions but completed all other items, and nine patients missed the last seven questions but completed all other items. This reflects the break in the page that the questionnaire was spread over, and likely reflects patients missing a page. The expectation questionnaire demonstrates a similar pattern for items 7 to 9 and items 10 to 12. A summary of item missingness for all scores can be found in Table 20.

Table 20: Missingness by item for score variables

Score	Number of items	Per cent missing
OKS	12	1.5%
Expectation	12	3 %
Helplessness	6	4.7%
Internality	5	4.7%
Depression	7	3.8%
Anxiety	7	3.7%
SF-36*	8	3.8%

**this figure represents the SF-36 domains.*

All the patterns of missingness are available in Figure 24 – of these missing value patterns, the 10 most frequent patterns are displayed in Figure 25. As was expected, the most common pattern identified was that of no missing values. All other patterns were infrequent.

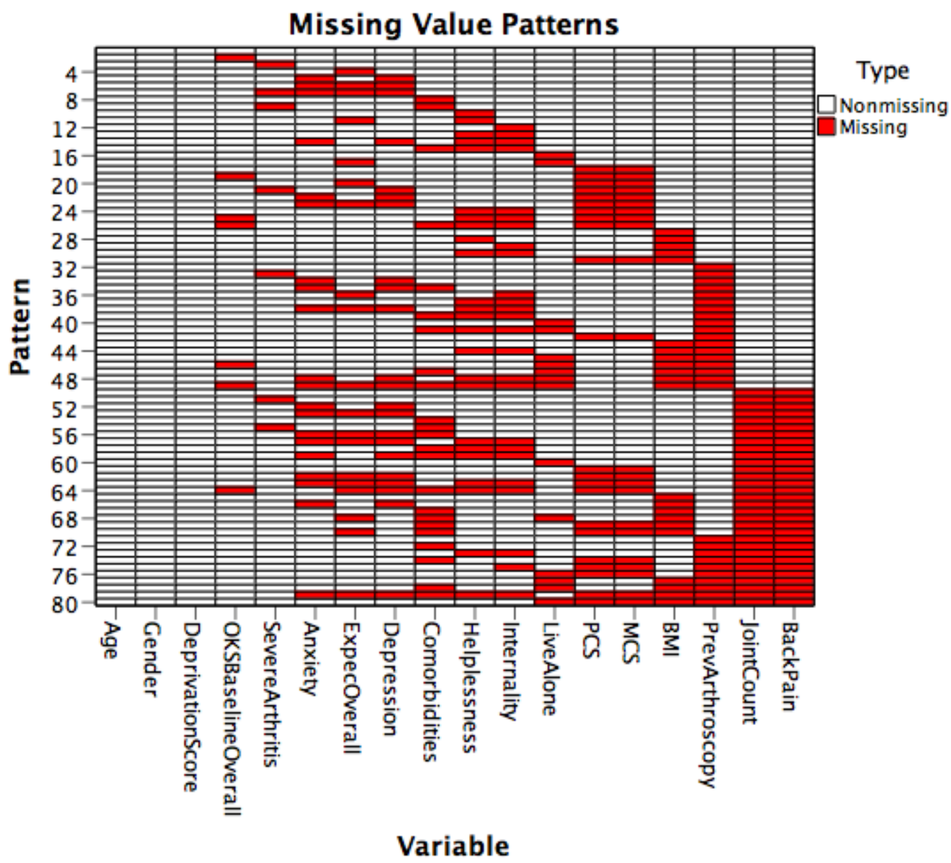


Figure 24: Patterns of missingness

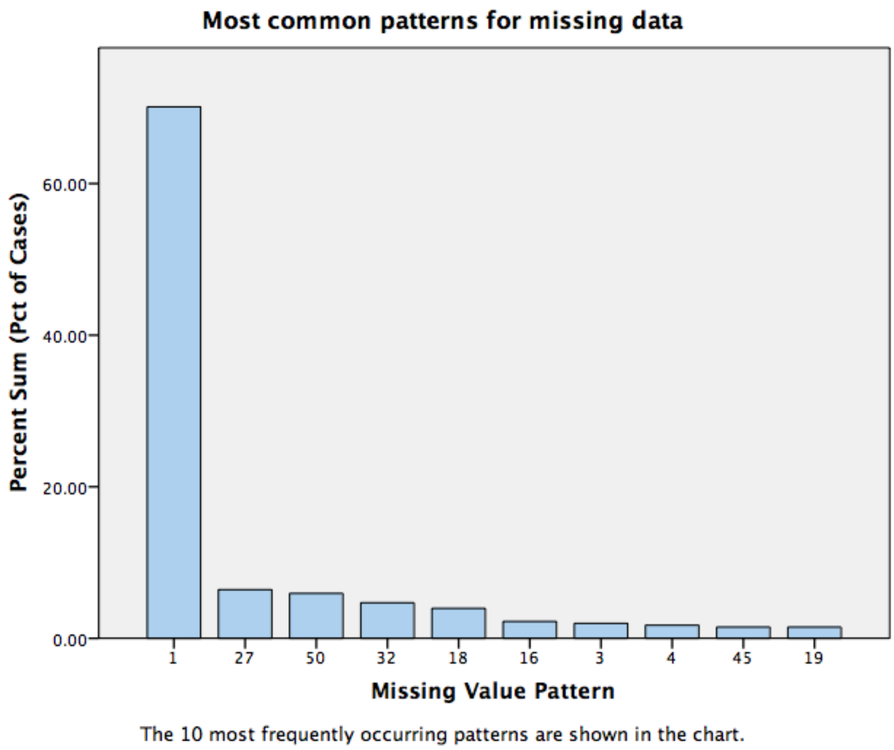


Figure 25: Frequency of the most common patterns of missing data

Handling missing data

The overall amount of missing data was low. Two patterns within the item missingness for scores emerged and likely reflected patients missing pages of the questionnaire. This mechanism accounts for a low proportion of missing items, and is unlikely to be non-ignorable (i.e. missing not at random; MNAR). Missing at Random (MAR) requires that "given the observed data, the missingness mechanism does not depend on the unobserved data". Given the likely cause for this pattern of missingness it seems reasonable to assume data are MAR, and as such conventional statistical modelling (e.g. regression analysis) is appropriate, with the expectation that resultant coefficient estimates and inferences will be unbiased, provided the appropriate variables are included in the models.

As a sensitivity analysis for this missingness pattern, models using a complete case analysis for all included explanatory variables in the final model (as opposed to a complete case analysis of all tested explanatory variables) and multiple imputation models were used.

7.2.5 Six Month Data analysis

At six months, 28 patients were lost to follow up, leaving 489 (94%) of eligible participants with complete OKS six month scores. All follow up took place after six months with a median of seven months (IQR=6 - 7.5). The median OKS score at six months was 36 (IQR=29 – 41), compared with the mean baseline score of 19.7 (sd=8.1)

Table 21 shows the results of a univariate analysis (Pearson correlation coefficients) between each explanatory variable and OKS at six months.

Table 21: Univariate correlation between each variables and six month OKS

Variable	6 month OKS	n	p-value
6 month OKS	1	489	.
Age	0.062	489	0.086
Female Gender	-0.07	489	0.061
OKS Baseline	0.336	475	<0.001
BMI	-0.142	432	0.001
Severe Arthritis	0.153	478	<0.001
Live Alone	0.044	454	0.177
Deprivation Score	-0.193	489	<0.001
Previous Arthroscopy (yes/no)	-0.039	425	0.214
Joint Count	-.294	429	<0.001
Low Back Pain	-.178	429	<0.001
Comorbidities	-.216	463	<0.001
Expectations	0.324	461	<0.001
Helplessness	-0.36	459	<0.001
Internality	-0.148	459	0.001
PCS	0.191	441	<0.001
MCS	0.428	441	<0.001
Depression	-0.327	463	<0.001
Anxiety	-0.283	464	<0.001

Assumption testing for linear model

Formal testing for independence of observations was not considered necessary because it was assumed that each case (person) was independent of the next. Linearity of associations between each explanatory variable and the dependent variable was informally assessed by scatterplots. Each scatterplot is presented in the appendix (section VI), and this assumption was thought to hold. Multicollinearity was assessed by entering all explanatory variables into a linear regression model in SPSS. This allowed the generation of Pearson's correlation coefficients between all variables. No variables had a correlation coefficient above 0.7; however, MCS and depression (0.59), MCS and anxiety (0.699), and depression and anxiety (0.549) were high. This collinearity between these measures was to be expected given that they are measuring similar psychological metrics. It was felt the assumption of non-collinearity was met (please see appendix section VI for correlation coefficients). The assumption of homoscedasticity of residuals (indicating the variance of the residuals is the same for all values of predicted variable) and normality of residuals were tested on the fitted model. The results of the homoscedasticity of residuals can be found in the residual versus prediction scatterplot in the appendix (section VI). Normality of residuals was assed informally using QQ plots and histograms, which are available in the appendix (section VI). Overall the assumptions required for a linear regression model were valid.

Model building

Before model building I decided that age, gender and OKS should be included as necessary parts of the model. This allows the model to be corrected for basic demographics and knee function of patients presenting for knee replacement. Complete case analysis (including cases that had not missing data for any variable tested in the modelling) was used, which allowed analysis of 271 cases.

Forward stepwise analysis, using a p-value of 0.05 for inclusion and 0.1 for exclusion, was then used for explanatory variable selection using SPSS version 22.[164] Examination of each included variable using drop one diagnostics was performed. The Akaike Information Criterion (AIC), which is a measure of how well a model fits the observed data and includes a penalty for the complexity of the model, was included in the drop one diagnostics.[165]

The variables age, gender, baseline OKS, MCS, expectations and depression were included in the model. Patients with higher baseline OKS, higher (better) MCS, higher expectations, and lower levels of depression have higher (better) OKS scores at six months. The model summary with no interaction terms is displayed below in Table 22. The fitted model characteristics were F (6, 265) = 22.2, p<0.001, R=0.579, R2=0.335, SE=7.7. (F (x,y) = the F statistic, with x representing the number of coefficients in the model, and y the degrees of freedom; R = correlation coefficient that when squared (R2) gives the amount of variability the model predicts; S.E – standard error of the regression which is the square root of the mean sum of squares residuals). The Adjusted R2 is 0.32 (this value corrects for the number of explanatory variables in the model). This means that the model describes 32% of the variability in outcome.

Table 22: Coefficients for first order fitted model (six month OKS)

Explanatory variable	z	Std. Error	95% CI Lower Bound	95% CI Upper Bound	Beta	t	p
(Constant)	10.557	6.787	-2.806	23.921		1.556	0.121
Age	-0.034	0.057	-0.147	0.079	-0.031	-0.593	0.553
Female Gender	0.844	0.993	-1.111	2.798	0.044	0.85	0.396
OKS Baseline	0.223	0.069	0.087	0.359	0.183	3.233	0.001
MCS	0.23	0.051	0.13	0.331	0.301	4.505	<0.001
Expectations	0.283	0.103	0.08	0.485	0.147	2.752	0.006
Depression	-0.527	0.201	-0.922	-0.131	-0.168	-2.621	0.009

z= the estimated regression correlation coefficient
Beta= the standardized regression correlation coefficient. This reflects the number of standard deviations the response variable will alter with one standard deviation change in the explanatory variable. These are directly comparable across explanatory variables.

Drop one diagnostics were used to assess relative contributions to the final model from each explanatory variable. This involves removing each variable from the model and assessing the model fit. When drop one diagnostics is used, the AIC can compare the two models. Models with a lower AIC fit the data better, taking into account the number of variables in the model. The results can be found in Table 23 where model terms are ordered in importance to the overall model fit. The model without age included provides a higher R2 of 0.322 and a lower AIC, suggesting a model that fits the data better. Similarly, gender provides a higher R2 of 0.321, with a lower AIC. All other variables contribute to the model with lower AIC and higher R2 when included. Depression provides the least amount of explanatory power (about 1.7% of the total variability the model can predict) whereas MCS provides the most (around 5% of the total variability the model can predict).

Table 23: Drop one diagnostics (six month OKS)

Model	R	R2	Adjusted R2	Std. Error of the Estimate	R2 Change	p	AIC
Full model	0.579	0.335	0.32	7.68496	-	-	1116.3
Age	0.578	0.334	0.322	7.67559	-0.001	0.553	1114.6
Female Gender	0.578	0.334	0.321	7.68094	-0.002	0.396	1115.0
Depression	0.564	0.318	0.305	7.76928	-0.017	0.009	1121.2
Expectations	0.562	0.316	0.304	7.7793	-0.019	0.006	1121.9
Baseline OKS	0.556	0.309	0.296	7.82027	-0.026	0.001	1124.8
MCS	0.533	0.284	0.271	7.95878	-0.051	<0.001	1134.3

R=Pearson's correlation coefficient; R2=Pearson's product moment correlation coefficient; Adjusted R2=R2 adjusted for the number of explanatory variables in model; AIC= Akaike Information Criterion, which is a measure of how well a model fits the observed data, including a penalty for the complexity of the model

Variables that were not significant in the final model

Deprivation was close to statistical significance (p=0.099) but was not include in the model. All excluded variables are displayed in Table 24.

Table 24: Excluded variables (six month OKS)

Explanatory Variable	z	t	p
BMI	-.052	-0.909	0.364
Severe Arthritis	.078	1.532	0.127
Joint Count	-.080	-1.404	0.161
Lower back pain	-.037	-0.701	0.484
Number of co-morbidities	-.023	-0.401	0.689
Live Alone	.045	0.855	0.393
Deprivation Score	-.085	-1.653	0.099
Previous Arthroscopy	.002	0.035	0.972
Helplessness	-.098	-1.564	0.119
Internality	-.018	-0.336	0.737
PCS	.066	0.897	0.371
Anxiety	.061	0.812	0.418

z=the standardised correlation coefficient (equivalent to Beta in the model tables) if this term were included in the model.

Interaction terms

Pairwise interaction terms were introduced into the fitted model and were selected using the same forward stepwise regression. Only terms that were already included in the model were introduced as interaction terms. All variables were mean-centred which allows easier interpretation of model coefficients (i.e. the model coefficients describe the effect of one explanatory variable on another's mean).

The interaction terms between depression and age, and expectation and gender were statistically significant model terms. To investigate the meaning of the interaction terms in more detail age was divided into three equal groups (50 to 65, 66 to 73, and 74 and over). This allowed us to plot the interaction terms of depression and age, and gender and expectation. Each variable was then plotted against predicted outcome (Figure 26 and Figure 27) to allow exploration of the relationship.

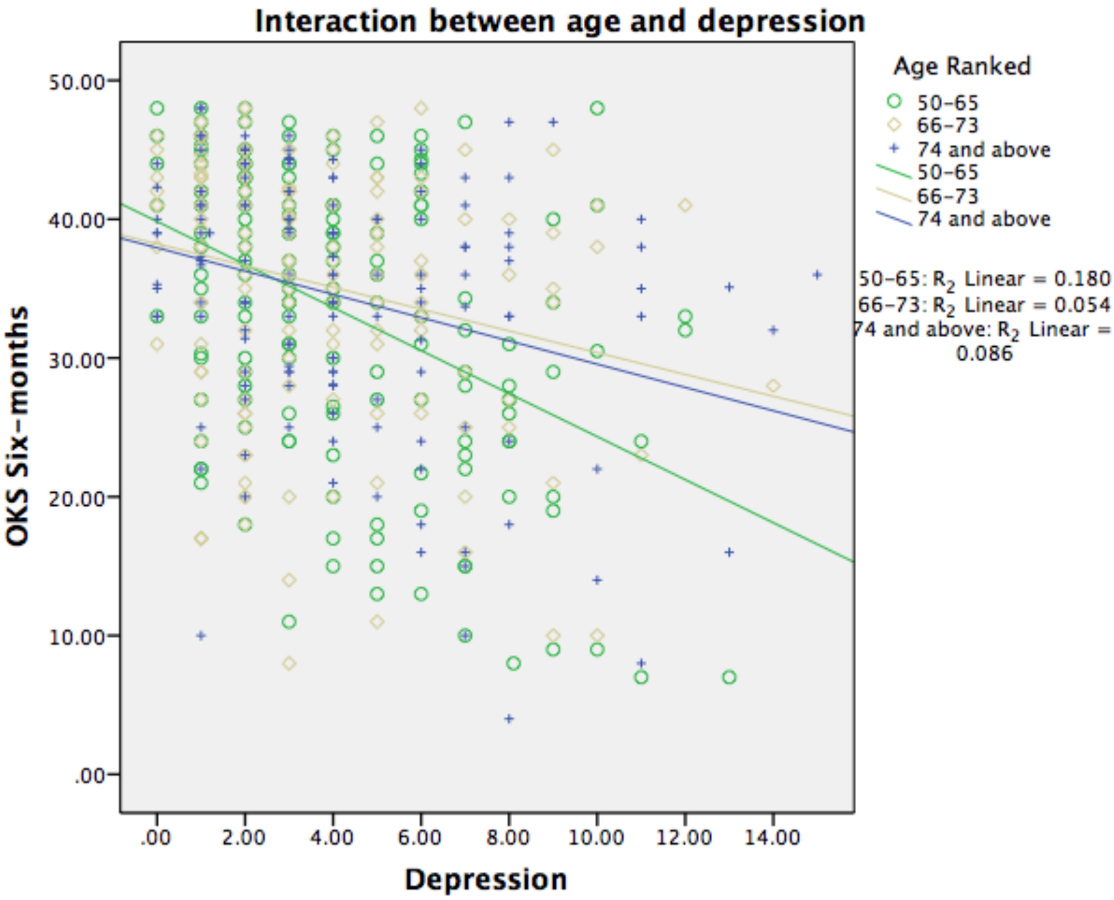


Figure 26: Interaction between age and depression

Age has little effect on the relationship between depression and OKS for low levels of depression. However, for higher levels of depression lower ages have worse OKS scores. This effect becomes more marked the higher the depression score. Depression has less of an effect on outcome in those aged 66 years and over.

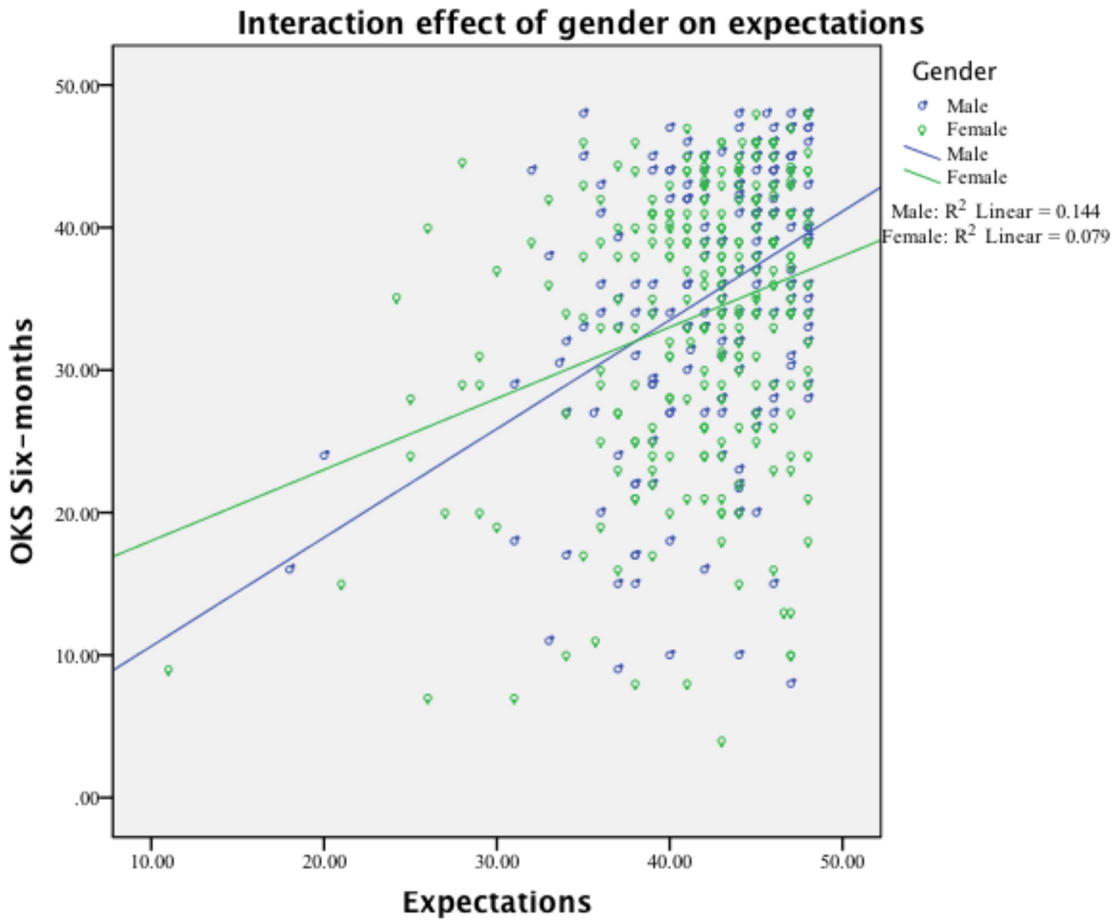


Figure 27: Interaction effect of gender and expectations

Males with low expectations demonstrate lower six month OKS scores than females with low expectations, but this relationship is reversed with high expectation (males with high expectations demonstrate higher six month scores that females with high expectations). Expectations have more of an effect on males than on females.

Variables that were not significant in the model

Table 25 demonstrates all excluded variables after the interaction terms were fitted. Severe arthritis (p=0.079) and the interaction term between depression and MCS (p=0.082) are very nearly significant predictors in the model with the significant interaction terms modelled.

Table 25: Excluded variables including interaction terms (six month OKS)

Variable	z	t	p
BMI	-0.052	-0.921	0.358
Deprivation Score	-0.075	-1.479	0.14
Comorbidity	-0.037	-0.655	0.513
Joint Count	-0.077	-1.358	0.176
Helplessness	-0.09	-1.446	0.149
Internality	-0.012	-0.219	0.827
PCS	0.064	0.878	0.381
Anxiety	0.048	0.646	0.519
Severe Arthritis	0.089	1.762	0.079
Lower back pain	-0.019	-0.375	0.708
Previous Arthroscopy	-0.002	-0.041	0.967
Live Alone	0.052	0.995	0.321
Interaction Gender/OKS	0.074	0.976	0.33
Interaction Gender/Age	-0.036	-0.44	0.661
Interaction Gender/MCS	0.099	1.063	0.289
Interaction Depression/Gender	-0.089	-1.154	0.25
Interaction Depression/MCS	0.095	1.745	0.082
Interaction Depression/Expectations	-0.046	-0.895	0.372
Interaction Depression/OKS	-0.054	-0.974	0.331
Interaction Expectations/OKS	-0.056	-0.994	0.321
Interaction Expectations/Age	0.031	0.603	0.547
Interaction Expectations/MCS	0.028	0.519	0.604
Interaction OKS/Age	0.015	0.294	0.769
Interaction OKS/MCS	-0.056	-1.071	0.285
Interaction Age/MCS	-0.036	-0.527	0.598

z=the standardised correlation coefficient (equivalent to Beta in the model tables) if this term were included in the model.

Drop one diagnostics

Drop one diagnostics were performed for all explanatory variables included in the model after the interaction terms were fitted. Table 25 displays the results. The inclusion of the interaction terms decreased the AIC, therefore all terms were included in the final model. Both interaction terms contribute around 1% of unique variability to the final model. No third order terms were included in the model, as it would involve including non-significant second order terms.

Table 26: Drop one diagnostics after inclusion of interaction terms

Model	R	R2	Adjusted R2	Std. Error of the Estimate	R2 Change	p	AIC
Full Model	0.599	0.359	0.339	7.57778	-	-	1110.6
Female Gender	0.597	0.357	0.34	7.57547	-0.002	0.36	1109.4
Age	0.597	0.356	0.339	7.57631	-0.002	0.344	1109.5
Expectations/Gender	0.591	0.349	0.331	7.62151	-0.01	0.045	1112.7
Depression/ Age	0.588	0.346	0.328	7.63887	-0.013	0.022	1114.0
Depression	0.586	0.344	0.326	7.6513	-0.015	0.014	1114.9
Expectation	0.576	0.331	0.314	7.72259	-0.027	0.001	1119.9
Baseline OKS	0.575	0.331	0.313	7.72657	-0.028	0.001	1120.2
MCS	0.559	0.312	0.294	7.834	-0.047	<0.001	1127.7

R=Pearson's correlation coefficient; R2=Pearson's product moment correlation coefficient; Adjusted R2=R2 adjusted for the number of explanatory variables in model; AIC= Akaike Information Criterion, which is a measure of how well a model fits the observed data, including a penalty for the complexity of the model

Final fitted model

The overall fitted model was F (8, 263) = 18.4, p<0.001, Adj R2 = 0.339 (R=0.599, R2=0.359) (SE=7.6). Regression coefficients, confidence intervals, and the proportion of unique variability each explanatory variable can account for can be found in Table 27.

Table 27: Coefficients of final model (six month OKS)

Variable	z	Std. Error	95% CI Lower Bound	95% CI Upper Bound	Beta	t	p
(Constant)	34.484	0.763	32.981	35.988		45.171	<0.001
Female Gender	0.902	0.984	-1.036	2.839	0.047	0.916	0.36
Age	-0.054	0.057	-0.166	0.058	-0.048	-0.948	0.344
Baseline OKS	0.232	0.069	0.097	0.368	0.191	3.387	0.001
MCS	0.221	0.051	0.122	0.321	0.289	4.377	<0.001
Expectations	0.497	0.149	0.204	0.789	0.258	3.345	0.001
Depression	-0.495	0.2	-0.889	-0.102	-0.158	-2.479	0.014
Interaction depression/ age	0.041	0.018	0.006	0.076	0.116	2.297	0.022
Interaction gender/ expectations	-0.388	0.193	-0.768	-0.009	-0.149	-2.014	0.045

z= the estimated regression correlation coefficient
Beta= the standardized regression correlation coefficient. This reflects the number of standard deviations the response variable will alter with one standard deviation change in the explanatory variable. These are directly comparable.

In summary:

- This model accounts for 33.9% of the variability found in OKS at six months.
- MCS accounts for the greatest amount of unique variability (almost 5%), with expectations and baseline OKS accounting for around 2.5%, and the other variables around 1% each. Age and gender have small, insignificant effects.
- Better baseline OKS, higher (better) MCS and higher expectations result in higher (better) six month OKS scores.
- Higher age and higher levels of depression result in lower (worse) OKS scores.

__Performance of prediction model__

A scatter plot of predicted values against actual values is presented below in Figure 28, with a 95% confidence interval for the mean (i.e. a population based estimate).

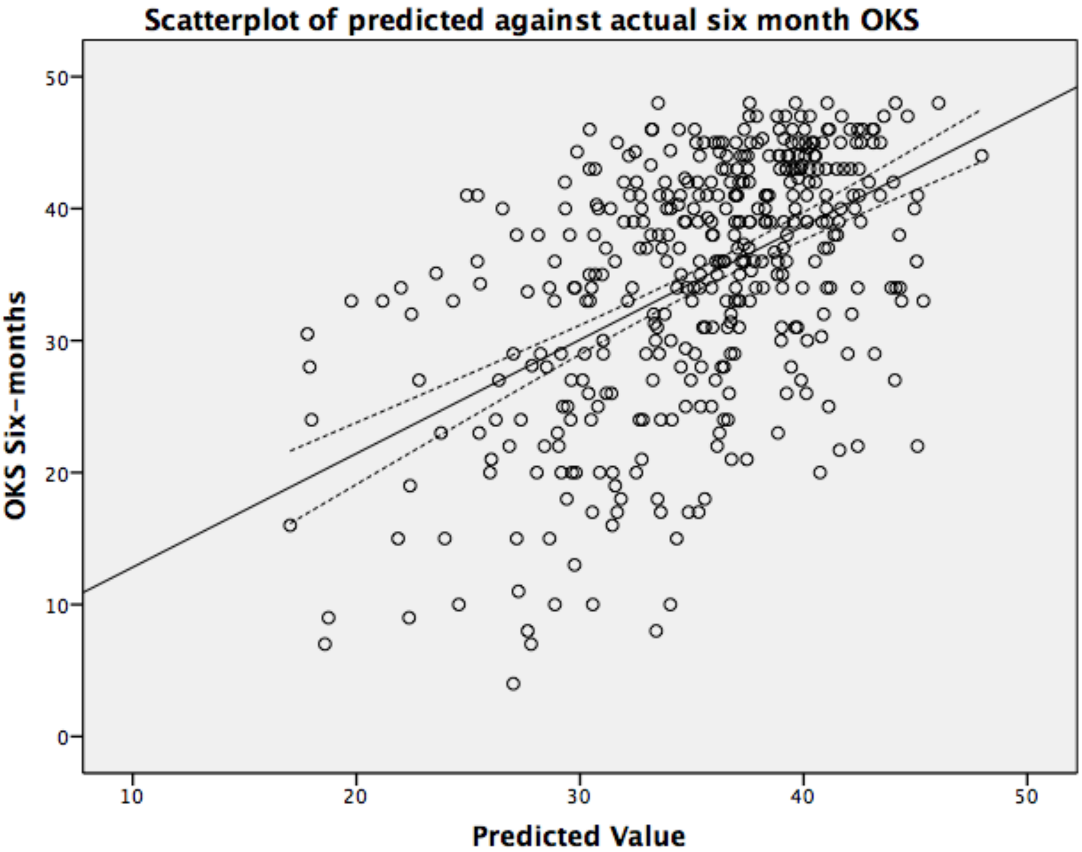


Figure 28: Predicted against actual six month OKS

When a 95% confidence interval for the individual is included, it is apparent that a large variation in actual against predicted scores would occur at the individual level (Figure 29). The usefulness of this model is discussed is section 8.2.

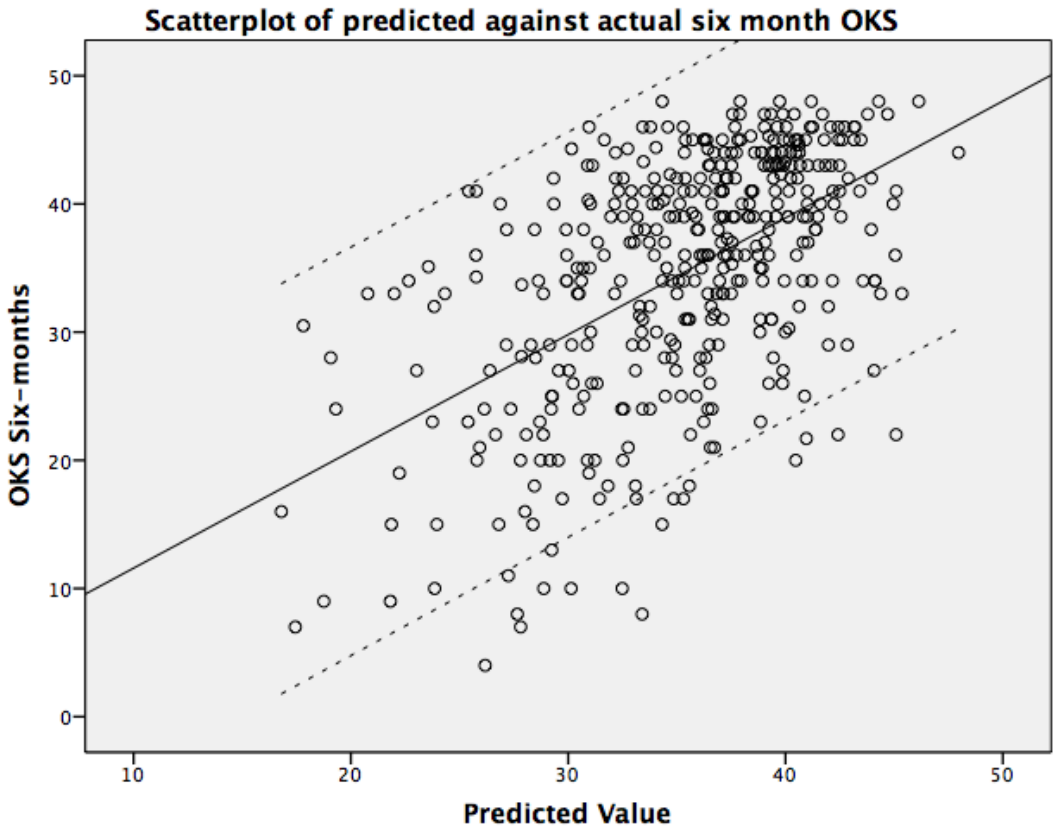


Figure 29: Actual against predicted six month OKS

Alternative outcome measures: OKS pain and function scores

Pain and function sub scores of the OKS may provide more useful models for prediction. An identical method of generating the final model was used as that of the full OKS score.

Pain subscale of OKS

The final model for pain was F (10, 261)=12.9, p<0.001, Adjusted R2=0.305 (R=0.575, R2= 0.331). Table 28 demonstrates a table of coefficients. Included variables were: age; gender; OKS (baseline); MCS; expectation; and depression (identical to the full model). Significant interaction terms were: depression and age; depression and expectation; depression and MCS; and gender and expectations. Therefore, this model included two interaction terms not in the full OKS six month outcome model. All effects were of similar magnitude and direction as those for the full OKS outcome score. This model did not represent any improvement on prediction over the model for the full OKS score.

Table 28: Coefficients with six month OKS pain as outcome

Variable	z	Std. Error	95% CI Lower Bound	95% CI Upper Bound	Beta	t	p
(Constant)	74.735	1.853	71.086	78.384		40.331	<0.001
Female Gender	4.315	2.259	-0.133	8.764	0.101	1.91	0.057
Age	0.014	0.131	-0.244	0.271	0.006	0.106	0.916
Baseline OKS	0.37	0.157	0.06	0.68	0.136	2.35	0.02
MCS	0.418	0.117	0.187	0.648	0.244	3.571	<0.001
Depression	-0.872	0.47	-1.798	0.054	-0.124	-1.855	0.065
Expectations	1.149	0.343	0.474	1.824	0.267	3.351	0.001
Interaction Age/ Depression	0.079	0.041	-0.002	0.16	0.101	1.932	0.054
Interaction Depression/ MCS	0.102	0.031	0.041	0.162	0.208	3.301	0.001
Interaction Depression/ Expectations	-0.178	0.07	-0.315	-0.041	-0.151	-2.556	0.011
Interaction Gender/ Expectations	-0.912	0.45	-1.798	-0.025	-0.157	-2.024	0.044

z= the estimated regression correlation coefficient
Beta= the standardized regression correlation coefficient. This reflects the number of standard deviations the response variable will alter with one standard deviation change in the explanatory variable. These are directly comparable.

Function subscale of OKS

Included terms when function alone was modelled were: age; gender; OKS (baseline); MCS; expectations; joint count; depression; interaction of joint count and MCS; and the interaction of gender and expectations. This altered from the full OKS score model by including joint count and the interaction between joint count and MCS, and excluding the interaction between depression and age. All relationships were in the same direction as the full model, with similar magnitude. Increasing number of joints being affected resulted in poorer functional outcomes, but only accounted for 0.5% of the unique variability predicted by the model. Overall the model accounted for 37.5% of the variability in functional outcome at six months.

The final model was $F (9,262) = 23.1$, $p<0.001$, Adjusted $R2 = 0.375$ ($R=0.629$, $R2=0.396$). Coefficients and confidence intervals for the final model are presented in Table 29. Figure 30 displays a scatterplot of actual against predicted functional scores, with 95% confidence intervals for individual scores.

Table 29: Coefficients with six month OKS function as outcome

Variable	z	Std. Error	95% CI Lower Bound	95% CI Upper Bound	Beta	t	p
(Constant)	69.872	1.645	66.633	73.111		42.475	<0.001
Female Gender	-0.686	2.086	-4.794	3.423	-0.017	-0.329	0.743
Age	-0.256	0.119	-0.49	-0.022	-0.107	-2.151	0.032
Baseline OKS	0.559	0.144	0.276	0.842	0.214	3.894	<0.001
MCS	0.382	0.108	0.17	0.595	0.232	3.541	<0.001
Joint Count	-0.576	0.401	-1.365	0.213	-0.088	-1.438	0.152
Expectations	1.054	0.313	0.438	1.669	0.255	3.37	0.001
Depression	-0.897	0.415	-1.715	-0.08	-0.133	-2.161	0.032
Interaction Gender/ Expectations	-1.054	0.406	-1.853	-0.255	-0.189	-2.598	0.01
Interaction Joint count/ MCS	0.047	0.022	0.005	0.09	0.125	2.195	0.029

z= the estimated regression correlation coefficient
Beta= the standardized regression correlation coefficient. This reflects the number of standard deviations the response variable will alter with one standard deviation change in the explanatory variable. These are directly comparable.

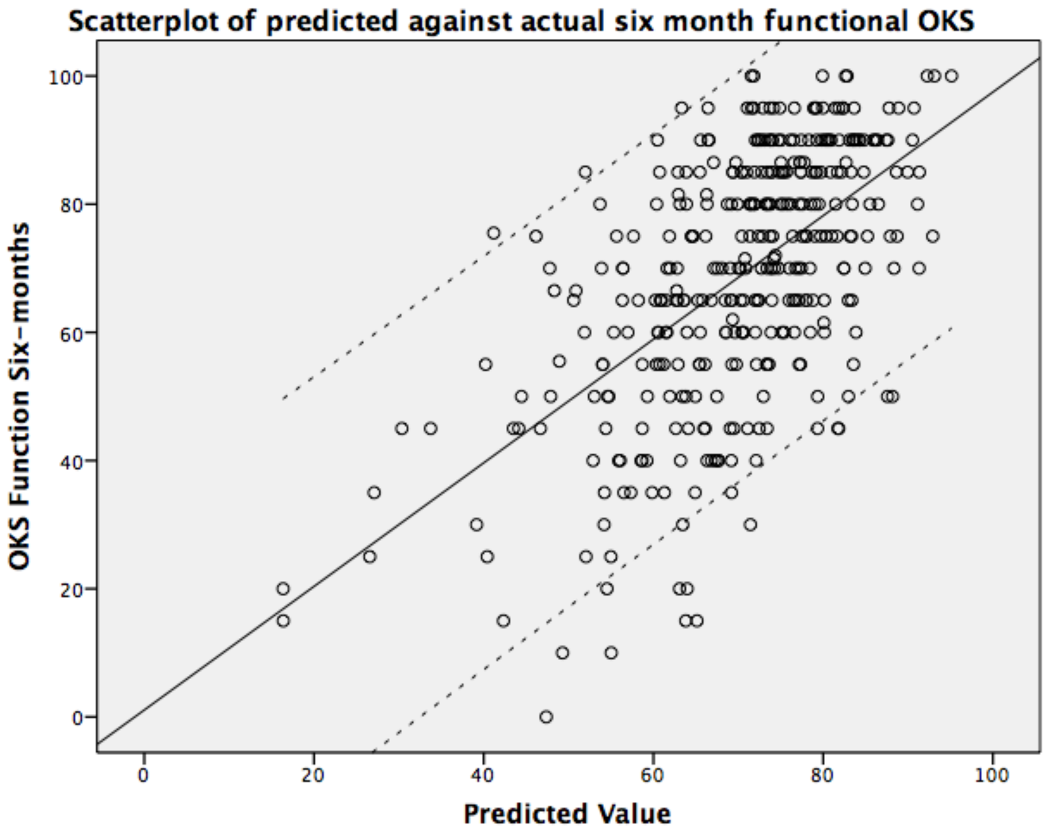


Figure 30: Predicted against actual functional scores at six months (OKS)

Usefulness of alternative outcome scores

Both pain and function sub scores of the OKS did not generate a more useful model than that provided by the complete score.

Sensitivity analysis – Multiple imputation

Multiple imputations by chained equations were used to provide 10 models with imputed data. This procedure was undertaken in SPSS and involves imputing missing data based on a regression model from known values combined with a random draw from the distribution of residuals. This process was repeated (in this case 10 times) to allow for variation in the randomly selected residuals. The final model for the OKS at six months was then fitted to the data. A model summary of each imputed case is presented in Table 30. Of note, when producing the model, complete case analysis of all explanatory variables (whether included in the model or not) was conducted. The procedure described here used a complete case analysis of all explanatory variables that were included in the final model, therefore included a larger proportion of the patients.

The pooled results for the imputed models (together with the original model coefficients for comparison) are given in Table 31. The pooled model was statistically significant ($p<0.001$), with $F(8,508)=25.251$, and an adjusted $R2$ of 0.264 (Standard Error=8.29).

The model fit is similar for the imputed data (27.6% of the variability), the "original data" (i.e. the complete case analysis of only those factors included in the model; 28.4% of the variability). The model fitting procedure, using only those cases that had complete data for all variables tested, whether included or not, could account for slightly more of the variability in that sample (33.9%); however the results are similar indicating the pattern of missingness is likely to be MAR.

Table 30: Model parameters for imputed data sets (six month OKS)

Imputation Number	R	R2	Adjusted R2	Std. Error of the Estimate	F statistic	p
Original data	0.546	0.298	0.284	8.02277	21.015	<0.001
1	0.538	0.29	0.279	8.29787	25.907	<0.001
2	0.537	0.289	0.277	8.41328	25.75	<0.001
3	0.562	0.316	0.305	8.2214	29.317	<0.001
4	0.532	0.283	0.272	8.34657	25.076	<0.001
5	0.531	0.282	0.271	8.29066	24.982	<0.001
6	0.549	0.302	0.291	8.18733	27.451	<0.001
7	0.544	0.295	0.284	8.22649	26.626	<0.001
8	0.537	0.288	0.277	8.19388	25.684	<0.001
9	0.5	0.25	0.239	8.52502	21.207	<0.001
10	0.53	0.28	0.269	8.41214	24.744	<0.001

R=Pearson's correlation coefficient; R2=Pearson's product moment correlation coefficient; Adjusted R2=R2 adjusted for the number of explanatory variables in model.

Table 31: Original and pooled coefficients for Multiple Imputation of six month OKS

Dataset	Variable	z	Std. Error	Lower Bound	Upper Bound	t	p
Original data	(Constant)	33.701	0.65	32.424	34.978	51.88	<0.001
	Age	0.036	0.048	-0.058	0.13	0.749	0.454
	Baseline OKS	0.18	0.057	0.067	0.293	3.123	0.002
	Expectations	0.499	0.136	0.231	0.767	3.665	<0.001
	MCS	0.231	0.043	0.147	0.315	5.411	<0.001
	Depression	-0.29	0.17	-0.625	0.045	-1.703	0.089
	Interaction gender/ expectations	-0.214	0.164	-0.536	0.109	-1.301	0.194
	Interaction depression/ age	0.033	0.015	0.005	0.062	2.28	0.023
	Female Gender	1.246	0.858	-0.441	2.932	1.452	0.147
Pooled	(Constant)	33.621	0.594	32.456	34.786	56.567	<0.001
	Age	0.043	0.045	-0.045	0.131	0.963	0.335
	Baseline OKS	0.189	0.054	0.084	0.295	3.514	<0.001
	Expectations	0.507	0.129	0.255	0.759	3.943	<0.001
	MCS	0.229	0.043	0.144	0.314	5.301	<0.001
	Depression	-0.221	0.164	-0.543	0.101	-1.345	0.179
	Interaction gender/ expectations	-0.183	0.158	-0.493	0.127	-1.16	0.247
	Interaction depression/ age	0.038	0.014	0.011	0.065	2.77	0.006
	Female Gender	0.975	0.79	-0.573	2.523	1.235	0.217

7.2.6 12 month data analysis

OKS

At six months, 38 patients were lost to follow up, leaving 480 (92.8%) of eligible participants with complete OKS 12 month scores. The median OKS score at 12 months was 39 (IQR=13), compared with the mean baseline score of 19.7 (sd=8.1). Two hundred and sixty-two patients were available for complete case analysis.

Table 32 shows the results of a univariate analysis (Pearson correlation coefficients) between each explanatory variable and OKS at six months.

Table 32: Univariate correlations of explanatory variables to 12 month OKS

Variable	Twelve Month OKS	n	p-value
Twelve Month OKS	1	480	.
Age	0.024	480	0.302
Female Gender	-0.052	480	0.13
OKS Baseline	0.394	465	<0.001
BMI	-0.165	423	<0.001
Severe Arthritis	0.108	465	0.01
Joint Count	-0.249	418	<0.001
Lower back pain	-0.192	418	<0.001
Number of co-morbidities	-0.248	450	<0.001
Live Alone	0.042	445	0.186
Deprivation Score	-0.238	480	<0.001
Previous Arthroscopy	-0.016	417	0.371
Expectations	0.326	454	<0.001
Helplessness	-0.382	450	<0.001
Internality	-0.201	450	<0.001
PCS	0.245	432	<0.001
MCS	0.429	432	<0.001
Depression	-0.326	455	<0.001
Anxiety	-0.302	456	<0.001

Model building

Assumption testing for 12 month OKS was identical to that described for 6 month OKS and results can be found in the appendix (section VI). Overall the assumptions required for a linear regression model were valid.

The process for building the model was identical to that described for the six month OKS.

The first order terms of age, gender, baseline OKS, MCS, and expectations were included in the final model (cf. the six month model that also included depression). The interaction term between gender and expectations was also included (cf. the six month model that also included the interaction between age and depression). The directions of all effects were identical to the six month model (better MCS, OKS, higher expectations, and female gender all lead to higher predicted 12 month scores). The interaction between gender and expectations was identical to that described for the six month data. Table 33 shows model coefficients.

The fitted model characteristics were $F (6, 256) = 21.5$, $p<0.001$, $R=0.579$, $R2=0.335$, $SE=7.8$. The Adjusted R2 is 0.32 (this value corrects for the number of explanatory variables in the model). This means that the model describes 32% of the variability in outcome.

Table 33: Model coefficients for 12 month OKS

Explanatory variable	z	Std. Error	95% CI Lower Bound	95% CI Upper Bound	Beta	t	p
(Constant)	35.311	0.789	33.758	36.865		44.767	<0.001
Female Gender	2.531	1.027	0.508	4.554	0.131	2.464	0.014
Age	-0.073	0.059	-0.189	0.044	-0.064	-1.23	0.22
Baseline OKS	0.293	0.071	0.153	0.433	0.24	4.118	<0.001
MCS	0.283	0.045	0.195	0.371	0.37	6.358	<0.001
Expectation	0.546	0.155	0.241	0.85	0.285	3.53	<0.001
Interaction Gender/ Expectations	-0.506	0.197	-0.895	-0.118	-0.198	-2.565	0.011

z= the estimated regression correlation coefficient
Beta= the standardized regression correlation coefficient. This reflects the number of standard deviations the response variable will alter with one standard deviation change in the explanatory variable. These are directly comparable across explanatory variables.

Drop one diagnostics were used to assess relative contributions to the final model from each explanatory variable. The results can be found in Table 34 where they have been organised in order of relative contribution. The model without age included provides a lower AIC, suggesting a model that fits the data better. All other variable contribute to the model with lower AIC and higher R2 when included. Age contributes the least explanatory power to the model (less than 1%), and MCS contributes the most at over 10%.

Table 34: Drop one diagnostics for 12 month OKS

Model	R	R2	Adjusted R2	Std. Error of the Estimate	R2 Change	p	AIC
Full Model	0.579	0.335	0.32	7.83	0.017	0.011	1089.6
Age	0.575	0.331	0.318	7.84	-0.004	0.22	1089.2
Female Gender	0.565	0.319	0.306	7.91	-0.016	0.014	1093.8
Interaction Expectations/Gender	0.564	0.318	0.305	7.92	-0.017	0.011	1094.3
Expectation	0.55	0.303	0.289	8.01	-0.032	0	1100.1
Baseline OKS	0.539	0.291	0.277	8.07	-0.044	0	1104.5
MCS	0.48	0.23	0.215	8.41	-0.105	0	1126.2

R=Pearson's correlation coefficient; R2=Pearson's product moment correlation coefficient; Adjusted R2=R2 adjusted for the number of explanatory variables in model; AIC= Akaike Information Criterion, which is a measure of how well a model fits the observed data, including a penalty for the complexity of the model

In summary the 12 month model:

- Predicts 32% of the variability in outcome
- Better (higher) MCS, better (higher) baseline OKS, higher expectations, and female gender all lead to higher predicted 12 month scores
- The MCS accounts for around 10% of the variability, with the baseline OKS accounting for around 5%.

OKS sub scores

The models for the OKS subscores did not improve greatly on the model for the complete score, accounting for 25% and 35% of the variability in outcome for the pain and function domains respectively. The coefficients are displayed below.

Pain

The final fitted model for 12 month OKS pain scores included age, gender, baseline OKS, MCS, and depression. No interaction terms were included. The model predicted around 25% of the variability in outcome. Table 35 shows the model coefficients.

Table 35: Model coefficients for 12 month OKS - Pain

Explanatory variable	z	Std. Error	95% CI Lower Bound	95% CI Upper Bound	Beta	t	p
(Constant)	76.707	1.812	73.138	80.276		42.325	<0.001
Female Gender	5.945	2.378	1.263	10.627	0.139	2.501	0.013
Age	-0.124	0.135	-0.39	0.142	-0.05	-0.917	0.36
Baseline OKS	0.535	0.16	0.22	0.85	0.198	3.341	0.001
MCS	0.533	0.122	0.293	0.773	0.316	4.381	<0.001
Depression	-0.963	0.476	-1.901	-0.025	-0.139	-2.022	0.044

z= the estimated regression correlation coefficient
Beta= the standardized regression correlation coefficient. This reflects the number of standard deviations the response variable will alter with one standard deviation change in the explanatory variable. These are directly comparable across explanatory variables.

Function

The explanatory variables included in the function model were identical to that of the model for the full OKS score. Directions of effects were similar and the overall amount of variability that could be explained by the model was similar at 35%. Table 36 shows the model coefficients.

Table 36: Model coefficients for 12 month OKS - Function

Explanatory variable	z	Std. Error	95% CI Lower Bound	95% CI Upper Bound	Beta	t	p
(Constant)	70.733	1.669	67.447	74.02		42.378	<0.001
Female Gender	2.858	2.171	-1.417	7.133	0.068	1.316	0.189
Age	-0.278	0.125	-0.523	-0.032	-0.113	-2.226	0.027
Baseline OKS	0.791	0.15	0.495	1.087	0.298	5.26	<0.001
MCS	0.532	0.094	0.346	0.717	0.32	5.643	<0.001
Expectations	1.221	0.327	0.577	1.865	0.294	3.732	<0.001
Interaction Expectations/ Gender	-0.931	0.418	-1.753	-0.108	-0.168	-2.227	0.027

z= the estimated regression correlation coefficient
Beta= the standardized regression correlation coefficient. This reflects the number of standard deviations the response variable will alter with one standard deviation change in the explanatory variable. These are directly comparable across explanatory variables.

SF-36 - PCS

The model building and testing of assumptions was identical for both domains of the SF-36 as for the OKS; however, age, gender and the baseline score of the dependent variable were included as co-variates (cf. age, gender and baseline OKS).

Fifty-eight patients (11.2%) did not have complete data at follow up (459 did; 88.8%). The mean score was 34.9 (sd=3.5), compared with a baseline mean score of 21.3 (sd=8.1). Two hundred and fifty-two patients were available for complete case analysis. The first order explanatory variables age, gender, PCS, MCS, comorbidity, BMI and expectations were included in the model, along with the interaction terms between gender/expectations and PCS/comorbidities. Of note, the interaction terms for Gender/MCS was excluded with a p-value of 0.052, and the first order explanatory variable OKS was excluded with a p-value of 0.092.

The overall fitted model was F (9, 243) = 20.6, p<0.001, Adj R2 = 0.411 (R=0.657, R2=0.432) (SE=10.5). Regression coefficients and confidence intervals can be found in

Table 37. Baseline PCS accounted for the most variability (8.4%), with gender accounting for the least (less then 0.1%).

Table 37: Model coefficients for SF-36 - PCS at 12 months

Explanatory variable	z	Std. Error	95% CI Lower Bound	95% CI Upper Bound	Beta	t	p
Female Gender	0.441	1.434	-2.383	3.265	0.016	0.308	0.759
Age	-0.251	0.088	-0.425	-0.077	-0.153	-2.842	0.005
PCS	0.51	0.085	0.342	0.678	0.309	5.973	<0.001
MCS	0.254	0.064	0.129	0.379	0.227	3.987	<0.001
Comorbidity	-1.783	0.495	-2.759	-0.807	-0.207	-3.598	<0.001
BMI	-0.382	0.128	-0.634	-0.131	-0.164	-2.993	0.003
Expectations	0.831	0.239	0.361	1.301	0.285	3.48	0.001
Interaction Gender/ Expectations	-0.835	0.301	-1.428	-0.242	-0.224	-2.775	0.006
Interaction PCS/ Comorbidity	0.114	0.052	0.012	0.216	0.113	2.204	0.028

z= the estimated regression correlation coefficient
Beta= the standardized regression correlation coefficient. This reflects the number of standard deviations the response variable will alter with one standard deviation change in the explanatory variable. These are directly comparable across explanatory variables.

This model indicates that better baseline PCS, MCS, higher expectations, lower BMI, fewer comorbidities, and lower age all predicted better outcomes.

Drop one diagnostics

Table 38 demonstrates the results from the drop one diagnostics for SF-36 PCS. The AIC for all variables is lower when that variable is included in the model, except for gender. This indicates that all variables included in the final model (apart from gender) improve the model fit.

Table 38: Drop one diagnostics for SF-36 - PCS at 12 months

Model	R	R2	Adjusted R2	Std. Error of the Estimate	R2 Change	p	AIC
Full model	.657	0.432	0.411	10.52845	0.011	0.028	1200.9
Female Gender	.657	0.432	0.413	10.5089	0	0.759	1199.1
Interaction PCS/ Comorbidity	.649	0.421	0.402	10.61132	-0.011	0.028	1204.0
Interaction Gender/ Expectations	.644	0.414	0.395	10.672	-0.018	0.006	1206.9
Age	.643	0.413	0.394	10.68007	-0.019	0.005	1207.2
BMI	.641	0.411	0.392	10.69873	-0.021	0.003	1208.1
Expectations	.636	0.404	0.384	10.76554	-0.028	0.001	1211.3
Comorbidity	.634	0.402	0.382	10.78305	-0.03	<0.001	1212.1
MCS	.629	0.395	0.375	10.84511	-0.037	<0.001	1215.0
PCS	.591	0.349	0.327	11.25168	-0.083	<0.001	1233.6

R=Pearson's correlation coefficient; R2=Pearson's product moment correlation coefficient; Adjusted R2=R2 adjusted for the number of explanatory variables in model; AIC= Akaike Information Criterion, which is a measure of how well a model fits the observed data, including a penalty for the complexity of the model

Interaction

The interaction effect between gender and expectations was similar to that described for both six and 12 month OKS. To explore the relationship between PCS and comorbidity, comorbidity was split into three approximately equal groups: up to 2 comorbidities (n=168), 3 comorbidities (n=145), and 4 and above comorbidities (n=175). Figure 31 shows this relationship: for up to 3 comorbidities there is a similar effect, with higher baseline PCS predicting higher 12 month PCS; patients with 4 comorbidities or more have lower PCS at 12 months when their baseline PCS is low, but higher PCS at 12 months when their baseline PCS is high. In other words, the PCS at 12 months in patients with high numbers of comorbidities were more affected by baseline PCS scores that for patients with low numbers of comorbidities.

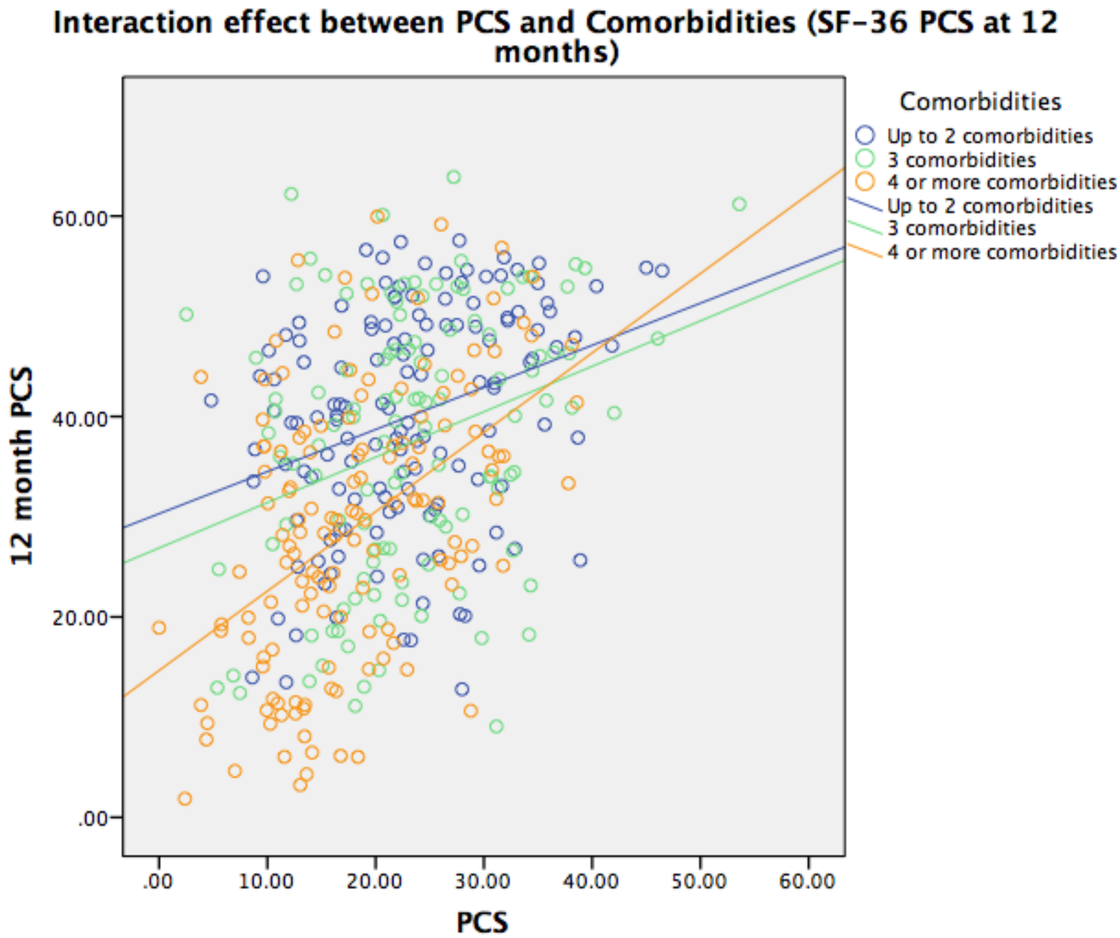


Figure 31: Interaction between PCS and comorbidities (SF-36)

In summary the full model for SF-36 PCS:

- Accounts for 41.1% of the variability in the PCS score at 12 months
- Baseline PCS accounts for the most individual variability (8.4%)
- Contrary to the OKS model, age is significant and predicts 1.9% of the variability in outcome.

Prediction

Figure 32 predicted (x-axis) against actual PCS scores at 12 months. A best fit line with 95% confidence intervals for individual values is included.

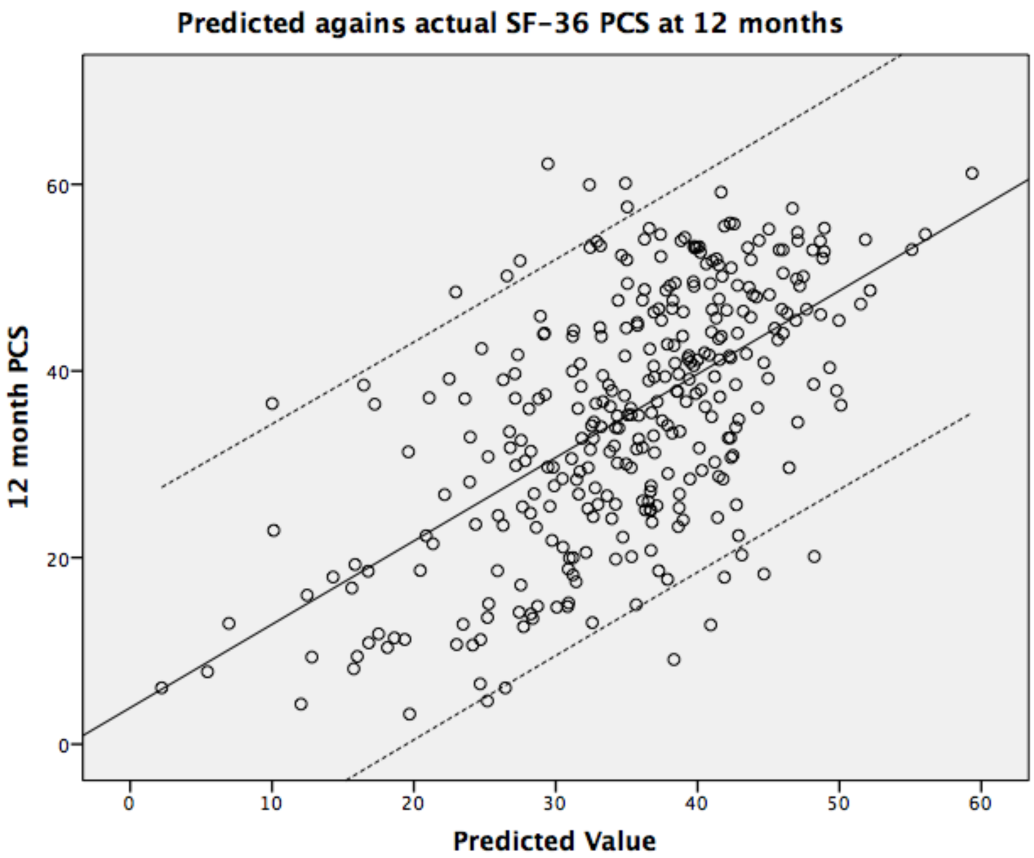


Figure 32: Predicted against actual SF-36 PCS

SF-36 - MCS

Fifty-eight patients (11.2%) did not have complete data at follow up (459 did; 88.8%).

The mean score was 52.1 (sd=10.1), compared with the baseline of 52.5 (sd=12.3).

Two hundred and fifty-two patients were available for complete case analysis. The first order explanatory variables age, gender, MCS, comorbidity, and depression were included in the model. No interaction terms were included. Of note, the explanatory variables of living alone (p=0.072) and anxiety (p=0.065) were excluded.

The overall fitted model was F (5, 247) = 33.9, p<0.001, Adj R2 = 0.395 (R=0.638, R2=0.407) (SE=8.3). Regression coefficients and confidence intervals can be found in Table 39. Baseline MCS accounted for the most variability (9.9%), with age accounting for the least (less then 0.2%).

Table 39: Model coefficients for SF-36 - MCS at 12 months

Explanatory variable	z	Std. Error	95% CI Lower Bound	95% CI Upper Bound	Beta	t	p
(Constant)	52.05	0.843		50.39	53.71	61.77	<0.001
Female Gender	1.165	1.098	0.054	-0.998	3.329	1.061	0.29
Age	-0.055	0.064	-0.043	-0.181	0.071	-0.864	0.388
MCS	0.363	0.057	0.419	0.252	0.475	6.432	<0.001
Comorbidity	-1.368	0.365	-0.205	-2.087	-0.649	-3.747	<0.001
Depression	-0.589	0.221	-0.167	-1.024	-0.154	-2.666	0.008

z= the estimated regression correlation coefficient
Beta= the standardized regression correlation coefficient. This reflects the number of standard deviations the response variable will alter with one standard deviation change in the explanatory variable. These are directly comparable across explanatory variables.

Drop one diagnostics

Table 40 demonstrates the results from the drop one diagnostics for SF-36 MCS. The AIC for all variables is lower when that variable is included in the model, except for age and gender. This indicates that all variables included in the final model (apart from age and gender) improve the model fit.

Table 40: Drop one diagnostics SF-36 MCS at 12 months

Model	R	R2	Adjusted R2	Std. Error of the Estimate	R2 Change	p	AIC
Full Model	0.638	0.407	0.395	8.27375	0.017	0.008	1075.2
Age	0.636	0.405	0.395	8.26953	-0.002	0.388	1073.9
Female Gender	0.636	0.404	0.395	8.27584	-0.003	0.29	1074.3
Depression	0.624	0.39	0.38	8.37498	-0.017	0.008	1080.3
Comorbidity	0.611	0.373	0.363	8.48848	-0.034	<0.001	1087.1
MCS	0.555	0.307	0.296	8.92171	-0.099	<0.001	1112.3

R=Pearson's correlation coefficient; R2=Pearson's product moment correlation coefficient; Adjusted R2=R2 adjusted for the number of explanatory variables in model; AIC= Akaike Information Criterion, which is a measure of how well a model fits the observed data, including a penalty for the complexity of the model

Prediction

Figure 33 shows predicted (x-axis) against actual MCS scores at 12 months. A best fit line with 95% confidence intervals for the mean is included.

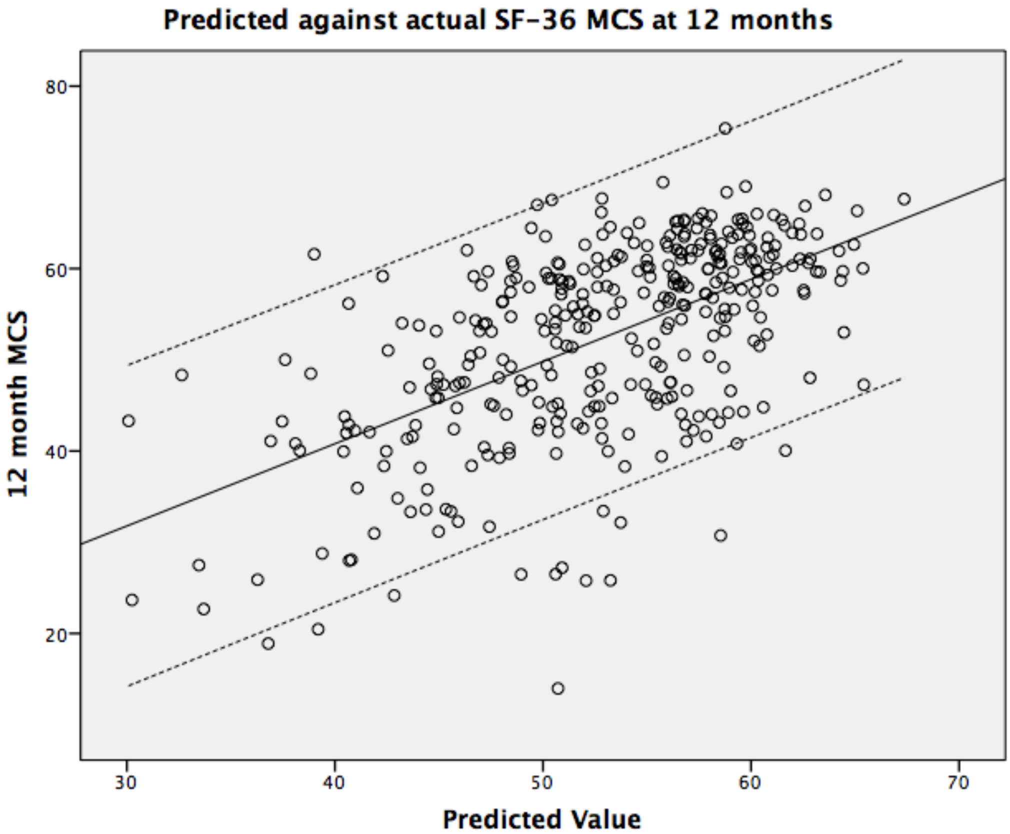


Figure 33: Predicted against actual SF-36 MCS

Satisfaction

Satisfaction was measured by a scale devised and validated by Mohmed.[157] Mahomed recommends analysis of the satisfaction score as a scale variable therefore linear regression was performed.

Fifty patients (9.9%) did not have complete data at follow up; 466 patients (90.1%) did have complete follow up data. The median score was 94 (IQR=25; Range=75). Two hundred and sixty-four patients were available for complete case analysis. The first order explanatory variables age, gender and OKS were covariates, with a stepwise procedure as described previously to model further terms. Depression and MCS were significant. Of note, the explanatory variable internality (p=0.056) was excluded. No interaction terms were significant.

The overall fitted model was F (5, 259) = 12.6, p<0.001, Adj R2 = 0.183 (R=0.446, R2=0.199) (SE=8.3). Regression coefficients and confidence intervals can be found in Table 41. Baseline depression and MCS accounted for the most variability in the model (3.8% and 3.7% respectively).

Table 41: Model coefficients for 12 month satisfaction

Explanatory variable	z	Std. Error	95% CI Lower Bound	95% CI Upper Bound	Beta	t	p
(Constant)	85.619	1.589	82.489	88.749		53.87	0
Female Gender	2.986	2.086	-1.121	7.094	0.084	1.432	0.153
Age	-0.042	0.12	-0.278	0.195	-0.02	-0.349	0.727
Baseline OKS	0.044	0.141	-0.233	0.321	0.02	0.314	0.753
Depression	-1.418	0.411	-2.228	-0.608	-0.246	-3.447	0.001
MCS	0.361	0.105	0.153	0.568	0.256	3.424	0.001

z= the estimated regression correlation coefficient
Beta= the standardized regression correlation coefficient. This reflects the number of standard deviations the response variable will alter with one standard deviation change in the explanatory variable. These are directly comparable across explanatory variables.

Model fit

The QQ plot demonstrates that the residuals were not normally distributed (left skewed). A common transformation to deal with left skewed data is to square or cube the response variable (Tukey's ladder of transformations).[165] Therefore, the response variable was squared and cubed, and models compared. The cubed model met the necessary assumptions for normality of residuals (QQ plots and histogram available in the appendix section VI).

The overall fitted model for satisfaction cubed included identical variables and was F (5, 259) = 13.7, p<0.001, Adj R2 = 0.196 (R=0.460, R2=0.212) (SE=64.3). Regression coefficients and confidence intervals can be found in Table 42. Baseline depression and MCS accounted for the most variability in the model (4% and 3.5% respectively). Therefore the model has only changed very slightly with the transformation.

Table 42: Model coefficients for 12 month satisfaction (cubed)

Explanatory variable	z	Std. Error	95% CI Lower Bound	95% CI Upper Bound	Beta	t	p
(Constant)	713371	26963	660270	766472		26.457	<0.001
Female Gender	41141	35385	-28543	110827	0.068	1.163	0.246
Age	-1097	2036	-5107	2913	-0.031	-0.539	0.591
OKS Baseline	1761	2385	-2935	6458	0.046	0.739	0.461
Depression	-25182	6980	-38929	-11436	-0.255	-3.608	<0.001
MCS	6038	1787	2517	9560	0.25	3.378	0.001

z= the estimated regression correlation coefficient
Beta= the standardized regression correlation coefficient. This reflects the number of standard deviations the response variable will alter with one standard deviation change in the explanatory variable. These are directly comparable across explanatory variables.

Drop one diagnostics

Table 43 demonstrates the results from the drop one diagnostics for satisfaction. The AIC for variables that were included as covariates (age, gender and OKS) is lower than that for the full model, indicating that they are not related to satisfaction. Only the variables MCS and depression improve the model fit.

Table 43: Drop one diagnostics for satisfaction

Model	R	R2	Adjusted R2	Std. Error of the Estimate	R2 Change	p	AIC
Full Model	0.46	0.212	0.196	266390.81	0.035	0.001	6502.1
Age	0.459	0.211	0.199	266019.78	-0.001	0.591	6500.4
Baseline OKS	0.458	0.21	0.198	266153.25	-0.002	0.461	6500.7
Female Gender	0.456	0.208	0.195	266574.52	-0.004	0.246	6501.5
MCS	0.42	0.177	0.164	271772.93	-0.035	0.001	6511.6
Depression	0.414	0.172	0.159	272595.25	-0.04	<0.001	6513.1

R=Pearson's correlation coefficient; R2=Pearson's product moment correlation coefficient; Adjusted R2=R2 adjusted for the number of explanatory variables in model; AIC= Akaike Information Criterion, which is a measure of how well a model fits the observed data, including a penalty for the complexity of the model

Decision regret

Decision regret was measured by a yes/no question:

"Knowing what you know now, would you still choose to have the operation on your knee"[158,159]

Four hundred and sixty-one patients (89.2%) responded to this question, with 50 patients reporting regretting having the procedure (10.8%).

Logistic regression was used to build a model to predict which patients were at high risk of decision regret. A similar model building strategy was used, with age, gender and OKS at baseline included within the model, and then a forward conditional stepwise procedure in SPSS used to add model terms. This procedure includes terms if they are significant, based on the Wald statistic.

Using complete case analysis 255 patients were included in the model, with 23 (9%) expressing decision regret.

The final model included the terms age, gender, OKS, depression, MCS and the interaction between age and gender. Model coefficients are demonstrated below in Table 44.

Table 44: Model coefficients for decision regret

Variables	B	S.E.	Wald	p	Odds Ratio	95% CI Lower Bound	95% CI Upper Bound
Age	-0.01	0.038	0.065	0.799	0.99	0.92	1.066
Female Gender	-7.638	4.171	3.352	0.067	0	0	1.713
Baseline OKS	0.028	0.033	0.684	0.408	1.028	0.963	1.097
MCS	-0.052	0.024	4.591	0.032	0.949	0.904	0.996
Depression	0.227	0.089	6.522	0.011	1.255	1.054	1.495
Age by Gender	0.121	0.06	4.035	0.045	1.128	1.003	1.269
Constant	-1.132	2.865	0.156	0.693	0.322		

Gender is for females compared to males; B=regression coefficient; S.E.- standard effort: Wald= Wald statistic

This table demonstrates that patients with poorer baseline MCS (low scores) and higher levels of depression (high scores) are more likely to express decision regret after their operation. The Nagelkerke R2 for this model was 0.221. A contingency table demonstrating the ability of the model to predict decision regret is shown in Table 45. The sensitivity of this model is 8.7%, and the specificity is 99.1%. The positive predictive value (predicting decision regret) is 50%, and the negative predictive value is 91.6%. Although this represents excellent specificity and negative predictive values, this is more a reflection on the low number of patients with decision regret.

Table 45: Contingency table of decision regret model

Observed	Predicted		Percentage Correct
	No regret	**Regret**	
No regret	230	2	99.1
Regret	21	2	8.7
Overall percentage			91

Assumption testing

Linearity of explanatory variables to logit of the response variable was tested using the Box-Tidwell procedure. The results are available in the appendix (section VI) demonstrating that this assumption was met.

7.2.7 Sensitivity analysis

Multiple imputations by chained equations were used to provide 10 models with imputed data. The final models for all outcomes at 12 months were then fitted to the data. Of note, when producing the linear regression models, complete case analysis of all explanatory variables (whether included in the model or not) was conducted. The procedure described here used a complete case analysis of all explanatory variables that were included in the final model, therefore included a larger proportion of the patients.

OKS 12 months

The model summary for each data set is given in Table 46.

Table 46: Imputation models for OKS 12 months

Imputation Number	R	R Square	Adjusted R Square	Std. Error of the Estimate	F statistic	p
Original data	0.539	0.291	0.28	8.30648	27.465	<0.001
1	0.511	0.261	0.252	8.58046	29.967	<0.001
2	0.505	0.255	0.246	8.50426	29.06	<0.001
3	0.502	0.252	0.244	8.46358	28.693	<0.001
4	0.509	0.259	0.25	8.53967	29.679	<0.001
5	0.495	0.245	0.236	8.56932	27.58	<0.001
6	0.52	0.271	0.262	8.45111	31.538	<0.001
7	0.517	0.268	0.259	8.58909	31.046	<0.001
8	0.505	0.255	0.246	8.55219	29.044	<0.001
9	0.509	0.259	0.25	8.54436	29.728	<0.001
10	0.512	0.263	0.254	8.50087	30.273	<0.001

R=Pearson's correlation coefficient; R2=Pearson's product moment correlation coefficient; Adjusted R2=R2 adjusted for the number of explanatory variables in model

The pooled results for the imputed models (together with the original model coefficients for comparison) are given in Table 47. The pooled model was statistically significant ($p<0.001$), with F (6,510)=32.41, and an adjusted R2 of 0.250 (Standard Error =8.53).

The model fit is similar for the imputed data (25.0% of the variability), the "original data" (i.e. the complete case analysis of only those factors included in the model; 28.0% of the variability). The model fitting procedure, using only those cases that had complete data for all variables tested, whether included or not, could account for slightly more of the variability in that sample (32%); however, a drop in R2 based from the development dataset (complete case analysis) to the pairwise and imputation datasets is to be expected. Additionally the correlation coefficients are a similar size and direction, indicating the pattern of missingness is likely to be MAR.

Table 47: Model coefficients (imputed and original) for 12 month OKS

Dataset	Variable	z	Std. Error	95% CI Lower Bound	95% CI Upper Bound	t	p
Original data	(Constant)	35.055	0.667	33.745	36.365	52.595	<0.001
	Female Gender	2.308	0.88	0.579	4.037	2.624	0.009
	Age	0.011	0.048	-0.084	0.106	0.229	0.819
	Baseline OKS	0.275	0.059	0.159	0.391	4.668	<0.001
	MCS	0.255	0.038	0.181	0.329	6.789	<0.001
	Expectations	0.484	0.14	0.209	0.759	3.456	0.001
	Interaction Gender/ Expectations	-0.245	0.167	-0.574	0.084	-1.464	0.144
Pooled	(Constant)	35.195	0.616	33.987	36.403	57.128	<0.001
	Female Gender	1.796	0.818	0.192	3.401	2.195	0.028
	Age	0.028	0.046	-0.062	0.118	0.61	0.542
	Baseline OKS	0.266	0.055	0.159	0.373	4.87	<0.001
	MCS	0.24	0.037	0.166	0.313	6.394	<0.001
	Expectations	0.46	0.131	0.203	0.718	3.504	<0.001
	Interaction Gender/ Expectations	-0.131	0.157	-0.439	0.177	-0.837	0.403

z=correlation coefficient

SF-36 PCS

The pooled results for the imputed models (together with the original model coefficients for comparison) are given in Table 48. The pooled model was statistically significant (p<0.001), with F (9,507)=27.69, and an adjusted R2 of 0.318 (Standard Error =11.24).

Table 48: Imputation models for SF-36 PCS

Imputation Number	R	R Square	Adjusted R Square	Std. Error of the Estimate	F statistic	p
Original data	0.598	0.357	0.34	10.99674	20.144	<0.001
1	0.564	0.319	0.306	11.37377	26.33	<0.001
2	0.569	0.324	0.312	11.18115	26.982	<0.001
3	0.586	0.343	0.332	11.16263	29.455	<0.001
4	0.567	0.322	0.31	11.33123	26.731	<0.001
5	0.569	0.324	0.312	11.13046	26.991	<0.001
6	0.581	0.337	0.326	11.23586	28.686	<0.001
7	0.571	0.326	0.314	11.21872	27.246	<0.001
8	0.566	0.321	0.309	11.19762	26.593	<0.001
9	0.593	0.352	0.34	11.17564	30.58	<0.001
10	0.571	0.326	0.314	11.36593	27.287	<0.001

R=Pearson's correlation coefficient; R2=Pearson's product moment correlation coefficient; Adjusted R2=R2 adjusted for the number of explanatory variables in model

The model fit is similar for the imputed data (31.8% of the variability) and the "original data" (i.e. the complete case analysis of only those factors included in the model; 34.0% of the variability). The model fitting procedure, using only those cases that had complete data for all variables tested, whether included or not, could account for slightly more of the variability in that sample (41.1%); however, a drop in R2 based from the development dataset (complete case analysis) to the pairwise and imputation datasets is to be expected. Additionally the correlation coefficients are a similar size and direction, indicating the pattern of missingness is likely to be MAR.

Table 49: Model coefficients (imputed and original) for SF-36 PCS

Dataset	Variable	z	Std. Error	95% CI Lower Bound	95% CI Upper Bound	t	p
Original data	(Constant)	34.624	1.008	32.641	36.607	34.349	<0.001
	Female Gender	1.024	1.305	-1.543	3.591	0.785	0.433
	Age	-0.188	0.078	-0.341	-0.034	-2.403	0.017
	MCS	0.25	0.055	0.142	0.358	4.541	<0.001
	Expectations	0.702	0.227	0.254	1.149	3.086	0.002
	Interaction Gender/ Expectations	-0.54	0.276	-1.082	0.002	-1.96	0.051
	PCS	0.463	0.075	0.315	0.611	6.151	<0.001
	BMI	-0.359	0.118	-0.591	-0.127	-3.044	0.003
	Comorbidity	-1.337	0.454	-2.23	-0.445	-2.949	0.003
	Interaction PCS/ Comorbidity	0.127	0.046	0.036	0.219	2.744	0.006
Pooled	(Constant)	34.413	0.861	32.722	36.104	39.978	<0.001
	Female Gender	0.957	1.108	-1.218	3.132	0.864	0.388
	Age	-0.128	0.065	-0.256	-0.001	-1.972	0.049
	MCS	0.256	0.05	0.157	0.355	5.09	<0.001
	Expectations	0.535	0.182	0.177	0.894	2.935	0.003
	Interaction Gender/ Expectations	-0.31	0.217	-0.735	0.116	-1.43	0.153
	PCS	0.472	0.064	0.346	0.598	7.344	<0.001
	BMI	-0.239	0.106	-0.447	-0.03	-2.253	0.025
	Comorbidity	-1.275	0.37	-2.002	-0.548	-3.445	0.001
	Interaction PCS/ Comorbidity	0.101	0.036	0.03	0.173	2.789	0.006

z=correlation coefficient

SF-36 MCS

The pooled results for the imputed models (together with the original model coefficients for comparison) are given in Table 50. The pooled model was statistically significant ($p<0.001$), with $F(5,511)=51.25$, and an adjusted R^2 of 0.327 (Standard Error =8.85).

Table 50: Imputed models for SF-36 MCS

Imputation Number	Model	R	R2	Adjusted R2	Std. Error of the Estimate	F statistic	p
Original data	1	.595	0.354	0.345	8.84345	40.911	<0.001
1	1	.572	0.327	0.321	8.89612	49.759	<0.001
2	1	.566	0.32	0.313	8.97588	48.062	<0.001
3	1	.578	0.335	0.328	8.75108	51.384	<0.001
4	1	.583	0.34	0.334	9.00654	52.654	<0.001
5	1	.559	0.313	0.306	8.92258	46.558	<0.001
6	1	.589	0.346	0.34	8.68916	54.178	<0.001
7	1	.579	0.335	0.329	8.85992	51.593	<0.001
8	1	.583	0.34	0.334	8.83908	52.655	<0.001
9	1	.576	0.332	0.326	8.86394	50.816	<0.001
10	1	.591	0.349	0.343	8.6983	54.876	<0.001

R=Pearson's correlation coefficient; R2=Pearson's product moment correlation coefficient; Adjusted R2=R2 adjusted for the number of explanatory variables in model

The model fit is similar for the imputed data (32.7% of the variability) and the "original data" (i.e. the complete case analysis of only those factors included in the model; 34.5% of the variability). The model fitting procedure, using only those cases that had complete data for all variables tested, whether included or not, could account for slightly more of the variability in that sample (39.5%); however, a drop in R2 based from the development dataset (complete case analysis) to the pairwise and imputation datasets is to be expected. Additionally the correlation coefficients are a similar size and direction, indicating the pattern of missingness is likely to be MAR.

Satisfaction

The pooled results for the imputed models (together with the original model coefficients for comparison) are given in Table 51. The pooled model was statistically significant ($p<0.001$), with $F(5,511)=14.45$, and an adjusted R2 of 0.115 (Standard Error =66.2).

Table 51: Model Coefficients for satisfaction (original and imputed)

Dataset	Variable	z	Std. Error	95% CI Lower Bound	95% CI Upper Bound	t	p
Original data	(Constant)	694872	22978	649697	740048	30.241	<0.001
	Female Gender	34252	30927	-26551	95056	1.108	0.269
	Depression	-19018	6045	-30903	-7133	-3.146	0.002
	MCS	5286	1549	2239	8332	3.412	0.001
	Age	1294	1722	-2092	4681	0.751	0.453
	Baseline OKS	2712	2026	-1270	6696	1.339	0.181
Pooled	(Constant)	693744	20675	653216	734272	33.555	<0.001
	Female Gender	26438	28010	-28498	81375	0.944	0.345
	Depression	-20443	5922	-32106	-8781	-3.452	0.001
	MCS	4658	1449	1816	7501	3.215	0.001
	Age	1617	1531	-1386	4621	1.056	0.291
	Baseline OKS	2204	1840	-1403	5812	1.198	0.231

z=correlation coefficient

Table 52 shows that the model fit is similar for the imputed data (11.5% of the variability) and the "original data" (i.e. the complete case analysis of only those factors included in the model; 13.2% of the variability). The model fitting procedure, using only those cases that had complete data for all variables tested, whether included or not, could account for slightly more of the variability in that sample (19.6%); however, a drop in R2 based from the development dataset (complete case analysis) to the pairwise and imputation datasets is to be expected. Additionally the correlation coefficients are a similar size and direction, indicating the pattern of missingness is likely to be MAR.

Table 52: Imputed models for satisfaction

Imputation Number	R	R2	Adjusted R2	Std. Error of the Estimate	F statistic	p
Original data	0.378	0.143	0.132	289866.2833	13.095	<0.001
1	0.364	0.132	0.124	289013.7349	15.563	<0.001
2	0.355	0.126	0.117	288396.8579	14.737	<0.001
3	0.347	0.12	0.112	292501.7304	13.956	<0.001
4	0.338	0.114	0.106	289883.7977	13.187	<0.001
5	0.345	0.119	0.111	291847.4735	13.852	<0.001
6	0.353	0.125	0.116	291381.5924	14.584	<0.001
7	0.364	0.133	0.124	287463.4821	15.632	<0.001
8	0.371	0.137	0.129	292653.5154	16.286	<0.001
9	0.336	0.113	0.104	290939.8146	13.021	<0.001
10	0.343	0.118	0.109	291779.944	13.651	<0.001

R=Pearson's correlation coefficient; R2=Pearson's product moment correlation coefficient; Adjusted R2=R2 adjusted for the number of explanatory variables in model

Decision regret

The individual classification tables for each model are given below (Table 53). Pooled model coefficients (along with the original model) are given in Table 54. Overall, the sensitivity of this model is around 2%. The model coefficients are similar and in a similar direction, suggesting the missing data is likely to be MAR.

Table 53: Classification table for decision regret (imputed data)

Imputation Number	Observed		Predicted		Percentage Correct
			Decision Regret		
			No regret	Regret	
Original data	Decision Regret	No regret	355	0	100
		Regret	38	1	2.6
	Overall Percentage				90.4
1	Decision Regret	No regret	459	0	100
		Regret	57	1	1.7
	Overall Percentage				89
2	Decision Regret	No regret	460	0	100
		Regret	56	1	1.8
	Overall Percentage				89.2
3	Decision Regret	No regret	462	0	100
		Regret	54	1	1.8
	Overall Percentage				89.6
4	Decision Regret	No regret	457	0	100
		Regret	59	1	1.7
	Overall Percentage				88.6
5	Decision Regret	No regret	455	1	99.8
		Regret	60	1	1.6
	Overall Percentage				88.2
6	Decision Regret	No regret	456	0	100
		Regret	60	1	1.6
	Overall Percentage				88.4
7	Decision Regret	No regret	462	0	100
		Regret	54	1	1.8
	Overall Percentage				89.6
8	Decision Regret	No regret	460	0	100
		Regret	56	1	1.8
	Overall Percentage				89.2
9	Decision Regret	No regret	455	0	100
		Regret	61	1	1.6
	Overall Percentage				88.2
10	Decision Regret	No regret	460	0	100
		Regret	56	1	1.8
	Overall Percentage				89.2

Table 54: Coefficients for decision regret (imputed and original)

	Variables	B	S.E.	Wald	p	Odds Ratio	95% CI Lower Bound	95% CI Upper Bound
Original data	Age	-0.027	0.026	1.087	0.297	0.974	0.926	1.024
	Female Gender	-4.418	2.976	2.205	0.138	0.012	0	4.112
	Baseline OKS	-0.006	0.025	0.067	0.796	0.994	0.946	1.044
	MCS	-0.046	0.018	6.455	0.011	0.955	0.922	0.99
	Depression	0.114	0.064	3.183	0.074	1.121	0.989	1.271
	Age by Gender	0.067	0.043	2.454	0.117	1.07	0.983	1.163
	Constant	1.339	2.004	0.446	0.504	3.815		
Pooled	Age	-0.02	0.022		0.36	0.98	0.939	1.023
	Female Gender	-2.77	2.745		0.315	0.063	0	14.183
	Baseline OKS	0.009	0.021		0.652	1.01	0.969	1.052
	MCS	-0.04	0.016		0.012	0.96	0.931	0.991
	Depression	0.114	0.058		0.05	1.121	1	1.255
	Age by Gender	0.039	0.039		0.316	1.04	0.963	1.123
	Constant	0.598	1.728		0.729	1.819	0.061	54.197

Gender is for females compared to males; B=regression coefficient; S.E.- standard effort: Wald= Wald statistic

7.3 Discussion

7.3.1 Summary of results

I have described the results of a multicentre cohort study designed to develop a prognostic model that characterises the association between pre-operative factors and outcome at six and 12 months. This study took place over six sites, with an estimated pool of 1500 patients, of which 999 were screened for inclusion. Six hundred patients were recruited, with 516 patients eligible for follow up at 12 months. Of those eligible for follow up over 90% completed follow up at six and 12 months. The linear regression models developed can:

- Predict 33.9% of the variability in OKS scores at six months
- Predict 32% of the variability in OKS scores at 12 months

The explanatory variables included in these models were similar, with similar effects: Poorer MCS scores (reflecting poorer mental health) resulted in poorer OKS scores, poorer baseline OKS scores resulted in poorer OKS outcome, and people with high expectations achieved higher OKS scores. Gender and expectations interacted, such that males with low expectation achieved lower scores than females, and males with high expectations achieved higher scores than females (i.e. expectations had a larger effect on males than on females). Age and gender did not lead to large changes in the models. Depression was a significant predictor in the six month model, but not in the 12 month model.

Multiple imputation techniques demonstrated that the models predict 27.6% of the variability at six months, and 25% of the variability at 12 months. This drop is to be expected, as the model was being expanded beyond the cases used to generate it.

Additional linear regression models were able to:

- Predict 41.1% of the variability in SF-36 PCS at 12 months
- Predict 39.5% of the variability in SF-36 MCS at 12 months
- Predict 19.6% of the variability in satisfaction at 12 months

Of the above models, the ability to predict PCS was the most promising. This was due to the MCS score changing very little from baseline (mean of 52.5 to 52.1), and the satisfaction linear regression model was unable to predict more than 20% of the variability.

The PCS model demonstrated a fall in the amount of variability it could predict to 31.8% when using multiple imputations. As discussed previously this is to be expected, and likely reflects the predictive power of the model in the general population more closely. The model indicates that better baseline PCS, MCS, higher expectations, lower BMI, less comorbidities, and lower age all predicted better outcomes. Interaction effects are similar between expectations and gender as that for the OKS model. This model accounts for a greater amount of variability than any of the other models.

A logistic regression model was used to predict patients at risk of decision regret. The model performance was disappointing, with a sensitivity of 8.7%, and a specificity of 99.1%. The positive predictive value (predicting decision regret) was 50%, and the negative predictive value was 91.6%.

7.3.2 Study validity

The external validity of the models presented depends upon the model covering a full cross section of patients it could be used on. I used representativeness of the study population as a proxy for this: the representativeness of the population screened; the representativeness of those patients that agreed to take part; and the representativeness of those patients included in the analysis. I investigated each of these mechanisms. The population screened and the population that took part closely reflected the general population of the UK that undergo knee replacement (data for the NJR) and the population of the hospitals included in the study, when compared across age and gender. Although there were some differences between some groups (e.g. between the baseline group of all knee replacements performed at all sites over the study period and those patients screened), the differences were small, the coding data used was of dubious quality, and the tests were very powerful. However, age and gender were included as covariates in all the models to allow correction for any differences. This approach does not account for potential selection bias in patients who refused to take part – indeed it is likely that the psychological profile of those agreeing and those refusing to take part is different.

The representativeness of the data analysed was tested though assessing the missingness patterns. Overall the study had low levels of missing data (6.5%), with good follow up rates of over 90%. Given the likely cause for this pattern of missingness I thought it reasonable to assume data are MAR. This allowed me to undertake conventional statistical modelling (e.g. regression analysis) with the expectation that resultant coefficient estimates and inferences will be unbiased, provided the appropriate variables were included in the models. The result of the multiple imputation analysis supports this assumption.

I used a complete case analysis as the primary analysis. This can result in bias,[165] and resulted in around 270 cases being used to build the model. This reduces the power of the analysis, and it is possible that factors that were significant were not included. However, given the point estimates of factors that were excluded for the model, I do not think they would have added a great deal to the predictive power, even if they were significant. A smaller sample size also leads to less precise estimates. To assess the missingness mechanism multiple imputation was uses, as described above. As expected the results of the multiple imputation revealed less predictive power from the models, but similar significance, size, and direction of effect for all coefficients.

7.3.3 Comparison with previous attempts at outcome prediction

Previous attempts at outcome prediction have predicted less than 20% of the variability. Currently, case mix adjustment used by the DoH uses pre- and post-operative factors and accounts for around a quarter of variability in OKS at six months. The variability that the models presented here can account for represent an improvement over the current methods; however, these models have not been validated on an independent sample of patients, and such validation is likely to produce estimates closer to the multiple imputation results that I have presented. This would account for around 27% of the variability in six month OKS, 25% of the variability in 12 month OKS, and 31% of the variability in 12 month PCS.

7.3.4 Does this model predict enough variability to be useful for individual outcome prediction?

The question of development of an outcome prediction tool from this prognostic model is a matter of judgment. Some would argue that any improvement in the pre-operative information available to patients is worthwhile, and while the amount of variability that is accounted for by the model is modest, it is in line with other prediction tools used to assist clinical decision-making in the NHS (e.g. the Framingham cardiovascular risk calculator accounts for around 30% of the variability in outcome).[167] The key to this question is to put it in context of the decision that is being made, and the knowledge and skills of the people making the decision. This thesis is concerned with informing individual patient decision-making (cf. the Framingham tool which is used to inform decisions around cardiovascular risk for the individual patient, with the expectation of improving population outcomes).

Therefore, it is a matter of judgement if individual prediction is worthwhile when the models reported here can account for around 30% of the variability in outcome. This means around 70% of the variability is unaccounted for: therefore, individual confidence intervals are still wide (around 80% as wide as for a model based only on the mean). Particularly for the primary outcome measure (the OKS at one year), the confidence interval for the individual that has the lowest prediction overlaps with the confidence interval for the individual that has the highest prediction. When we consider that the baseline OKS alone accounts for around 15% of the variability in outcome, it seems unlikely that we can justify the use of this tool in clinical practice for the purpose of informing individual patient choice. The additional variability that can be explained by the model is, in my opinion, unlikely to change patients' decision-making (i.e. we know that patients with low baseline OKS scores are unlikely to achieve high post-operative OKS scores, and patients with high baseline OKS scores are likely to achieve high post-operative scores; therefore the additional information that can be provided is limited). Additionally, chapter 4 described concerns from patients over the reliability of any information that a tool provided. With individual confidence intervals being as large as they are, it is unlikely patients would respond well to the accuracy of the model – the optimism bias suggests that patients would tend to favour their own chances of having a good outcome. Therefore the wide confidence intervals are likely to result in patients assuming they would be the small proportion that are at the higher end of the interval for a prediction of poor outcome. Furthermore, these models have not been validated on an independent sample of patients, and it would be expected that the performance of the model would be poorer on an external sample.

The models presented here present a step forward in the amount of variability that can be explained by pre-operative factors. However, based on the findings from Chapter 3 and 4, I do not think they provide the basis for individual prediction. This opens up the opportunity to use this model in different ways, and prompts further investigation into additional factors that can predict more variability.

7.3.5 Other applications for the model

Rationing of care

The effects of an outcome prediction tool are dependent on how it is used: medical professionals, commissioning groups, and surgeons could use it to ration care (i.e. not offering knee replacements to patients at high risk of worse outcomes). A form of rationing has been present in the NHS for some time, with some commissioning groups limiting access to knee replacements based on knee function scores and BMI.[25] Although rationing care by blocking access to certain groups of patients could be a feasible application of this work, it is not its aim. However, the model presented here would be an improvement on the current situation of rationing care based on baseline knee scores but, as discussed previously, the confidence intervals around individual prediction are wide, and therefore this approach is, in my option, open to question. Indeed, many in the orthopaedic community have questioned the usefulness of using rationalisation based on OKS scores, and these arguments are valid here.[168] Additionally, regardless of the current rationing practices, predicting outcome has ethical consideration: is it ethical to limit access to a treatment based on an outcome prediction tool, especially when those that are likely to have poorer outcomes still improve significantly, and the individual confidence intervals of the prediction are still wide (even if the population level confidence interval is relatively narrow)? Also, removing the patient from the decision-making process is ethically questionable, and is against current political movement in the NHS towards shared decision-making.[28,46,50]

Use of model for case mix adjustment

The Department of Health could incorporate this prognostic algorithm into their case mix adjustment for PROMs (described in chapter 5). Case mix adjustment for PROMs, based on pre-operative *and* post-operative factors, has been introduced as part of the best practice tariff from April 2015.[169]

The research presented here is aimed at informing the decision-making process of the patient with an outcome prediction tool. However, future work combining peri- and post-operative factors to the pre-operative model may produce a case-mix adjustment that can account for more variability than currently used (the DoH uses a case mix adjustment tool based on NJR and HES data that predicts around a quarter of the six month OKS). I would expect the model presented here to have roughly the same predictive power as the current case mix tool; however, this leads to the question of how much variability could be predicted if everything in the literature were combined with those factors described here? It is unlikely there would be much improvement given the factors not included in our model do not add a great deal of explanatory power, and that explanatory power is unlikely to be additive.

Additionally, a fairly modest improvement in the power of the case mix adjustment model would require a significant investment in time and money: the costs associated with licences around the SF-36 questionnaire (although the SF-36 RAND questionnaire is licence-free, it was not used in this model building, so further work would be needed to assess it); larger amount of data collection; new studies validating the work done here; further studies to combine pre- and post-operative explanatory variables; and an increase in patient burden. Assuming no interaction between terms included in previous models and the models presented here, there would be around a maximum of 9-10% increase in the variability accounted for (although interaction is highly likely). The improvement is therefore unlikely to justify the time and expense required to achieve it.

Finally, predicting around 30% of the variability may not be sufficient, as 70% of the variability is still unaccounted for. This means that trusts may get rewarded or penalized on the basis of this uncorrected and unaccounted variability.

Targeting factors that have been identified as predictive of outcome

This study, combined with the studies discussed in Chapter 5, provide a basis for studies aimed at modifying prognostic factors in an effort to improve outcomes. Some efforts in this area are already going on, for example the HAPPiKNEES study being conducted through Nottingham University is examining Cognitive Behavioural Therapy to address depression and anxiety before knee replacement.[96] This type of study could target each of the modifiable prognostic factors identified by the prognostic model.

It may be that such interventions change outcome by a small amount, and large trials would therefore be needed to demonstrate any improvement. Traditionally trials in medicine are focused on interventions that result in a predefined change in the outcome measure (e.g. the Minimally Clinical Important Difference: the smallest difference that a patient identifies as important).[165] As such, such trials may not detect a small change, or if they do it may not result in widespread adoption.

An alternative approach would be going down the route of "marginal gains". This idea was popularised by Sir Dave Brailsford, the British Cycling Performance director:

"If you broke down everything you could think of that goes into riding a bike, and then improved it by one per cent, you will get a significant increase when you put them all together,"

It may be that additive changes to modifiable predictive factors can improve outcome; however, this would require a large amount of investment to demonstrate efficacy.

7.3.6 Other factors that could be responsible for the (unaccounted) variation in outcome

There is currently a large amount of variability that is not accounted for. As a knee replacement is a complex intervention, there are many areas that introduce this variability:

- Pre-admission care. Pre-operative classes are commonplace in orthopaedic units, with some evidence of benefit.[170] It may be that certain pathways are better than others, or that some patients respond to some pathways differently.
- Admission care. Organisational issues, surgical technique, and anaesthetic type are all factors that could influence outcome.[170]
- Post-admission care. There are currently trials ongoing to assess the effect of different post-operative regimens on patients at high risk of poor outcomes.[151,153]
- The patient. There may be factors that I have not measured (e.g. catastrophisation, or biochemical factors) that influence outcome. To enable greater ability to predict, more in-depth analysis may be required (e.g. in-depth psychometric testing). Given feedback from participants in this study, running a study with a larger patient burden may result in difficulties in patient recruitment.
- Pathology. A large number of the population have OA of the knee. It may be that the diagnosis of "OA knee" does not reflect one pathological process, but may reflect a heterogeneous group of conditions with a similar pathological endpoint.[1,3,7] These different conditions could react differently to joint replacement.

Of the factors above, some exciting work is being conducted on humeral reactions to operation, stress, and cell signalling.[171-173] Of specific note is the preliminary work emerging from Stamford, USA on cell surface antigens and intracellular signalling in immune cells.[172,173] These finding (based on small sample sizes) suggest that they could account for over 50% of the variability in outcome. Combining these biomarkers with the patient factors described in this thesis could be a productive avenue of research. Additionally, several trials on post-operative rehabilitation procedures are ongoing.[151,153]

It is feasible that in the future meaningful prediction will be possible; this may represent individual prediction, or risk stratification (i.e. allocating patients into different risks of having poorer outcomes).

Chapter 8: Conclusions

In this thesis I set out to understand the factors important to patients when contemplating a knee replacement, how an outcome prediction tool could affect that process and what patients would want from such a tool. I then went on to identify prognostic factors and perform a multicentre cohort study to develop a prognostic algorithm that could help patients make a decision about progressing to a knee replacement. Such an algorithm could have uses outside of supporting individual patient decision-making, and those uses have been discussed.

To begin, I performed a systematic review of factors that influence patients' decision-making. I identified 17 individual themes across seven studies that included patients from the period of developing symptoms through to recovery after knee replacement. Understanding the factors that affect a patients' decision-making when considering a knee replacement is essential to the shared decision-making process and can act as a framework for understanding common concerns patients have. However, this review was unable to provide a model of decision-making that is theoretically grounded, and was also deficient in that individual studies did not include patients at different parts of the decision-making process.

I proceeded to report an original qualitative research project that developed a model of decision-making. I identified nine major themes that were important to patients when contemplating a knee replacement: stress of deliberation; expectation of outcome; sources of information; personal situation; mental state; coping strategies; loss of control; trust in doctor; and preferred model of care. The themes interacted comprehensively with one and other, the result being a complex interplay of factors that affect the deliberation process, the threshold to decision-making, and the ultimate decision. Interestingly there was a general preference for “bottom line” information married to a paternalistic decision-making process. This is in contrast to current political movements within the profession. Additionally, once the decision was made, patients were unlikely to revisit it, as there was stress associated with the deliberation for the decision.

An awareness of the deliberation phase, the factors that influence it, the stress associated with it, preferred models of care, and the influence of the decision-making threshold will aid useful communication between doctors and patients. Future work, examining how this information might be best translated and utilised in the clinical environment is an exciting avenue. This is one of the key elements in addressing the three crucial areas set out in the introduction: differences in utilisation rates,[31] a high dissatisfaction rate[25] and increasing demands with financial constraints.[27]

I then went on to conduct a qualitative analysis of how providing predictions of outcome could affect expectations and decision-making. This work developed our understanding of the effects predicting outcome could have on patients, and demonstrated that the effect of an outcome prediction tool is to a degree dependent on the content and presentation, the point in the pathway it is used, and whether it is delivering “good” or “bad” news. Work assessing the effect of PDAs would suggest a decrease in the proportion of people progressing to elective surgery could be expected. Additionally how the tool is delivered is likely to be key (i.e. as part of a shared decision-making model or part of a paternalistic model). These uncertainties will need careful evaluation if and when such a tool becomes available.

Additionally, this aspect of the thesis demonstrated that the timing of delivery of predictive information, along with the optimism bias, would have an effect on any future tool capable of predicting outcome. The optimism bias may mean that the effect on satisfaction rates that are hoped for with outcome prediction may not be realised. This effect may mean that any outcome prediction tool may need to have tight confidence intervals at the individual level, as any uncertainty is likely to be used to justify higher expectations. There was also concern that some patients may see it as a guarantee of outcome (rather than a prediction). Linked to this is the preference for information from friends and family. Conflicting information from a prediction and a family member who has had the operation is likely, and it appears that patients would prefer to hear from someone who has been through the procedure. This may mean that a completely different approach to presenting information is required: for example, a database of patient experience from patients that have had a knee replacement that can be matched to the baseline characteristics and likely outcome of a patient considering a knee replacement. Additionally, the effect of a tool on managing expectations and patient decision-making will alter depending on the point in the pathway it is used (patients who have already made up their mind appear less willing to change it based on new information – this could be due to the stress that is felt from the deliberation process). However, it is clear that patients welcome such information, and that it would appear to still have an effect on expectation and decision-making, especially if targeted early in the patient pathway.

Future work of any prediction tool would require examination of how big an effect the optimism bias would have, and how big an effect modifying expectations pre-operatively would have on satisfaction.

The next step in the body of work was a systematic review of the literature surrounding patient factors that affect outcome, in which I identified several candidate predictors. These included pre-operative knee status, psychological wellbeing and medical comorbidity. The review demonstrated that no single study has sought to measure them all within the same cohort, and therefore it was unknown how much variability could be predicted if all were combined.

Using the candidate prognostic factors identified in the systematic review I developed a multicentre cohort study designed to generate a prognostic algorithm. This study recruited 600 patients, and the linear regression model accounts for:

- 33.9% of the variability in OKS scores at six months
- 32% of the variability in OKS scores at 12 months
- 41.1% of the variability in SF-36 PCS at 12 months

These models explain more of the variability in outcome of total knee replacement for OA knee than any previously described model. However, widespread clinical use for individual prediction is probably not warranted. This opinion is based on the poor precision of the individual estimates, combined with the results from the qualitative work. Although there is an obligation to ensure patients are well informed before their operation, it seems likely that predictions with wide confidence intervals will not be as useful to patients as a report from someone that has had the procedure (especially when considering the optimism bias and the preference for information from friends and family). It may be that a future algorithm that can provide more precise estimates should be presented by using a database of past patient experiences, and matching that to current patients' predictions.

Future work should be aimed at several areas including attempting to modify prognostic factors that have been identified in this and previous work,[96,151,153] and identifying further potential prognostic factors that could improve the precision of the individual estimates. Once a model with sufficient explanatory power is developed (the definition of which is subjective) external validation and impact assessment can follow.

I have also discussed rationing care and case mix adjustment, the latter particularly relevant with the advent of Best Practice Tariffs based on adjusted outcome scores. The allocation of funds based on case mix adjustment that can only account for 25% of the variability in outcome is, in my opinion, unsound, and the models presented here, although likely to be an improvement, do not offer such an advance as to warrant the extra burden. Rationing care through a prognostic model is a potential use for this work, but the additional cost, requirement for transparency, ethical and political motivations, and patient views (brought out in the qualitative interviews) may make this a problematic area for future research.

Future areas that have the potential to provide greater explanatory power have been discussed. Humoral factors, stress, and resilience are promising, if poorly understood, areas. It seems likely that in the future more precise outcome prediction will be possible; it remains to be seen if such models will be precise enough to effectively aid patient decision-making and improve outcomes.

8.1 Future work

Future work is required identifying further explanatory variables that can account for variability in outcome. There are various factors that are under investigation currently and with these variables included in a prediction algorithm, individual prediction of outcome is likely. However, this does lead to two questions. The first is that perhaps there are many factors that account for a very small amount of variability each, and that the development of a prognostic algorithm will be too time-consuming and resource-rich to ever achieve. Until current promising areas of research have been explored this will be unknown. If this is the case, it may be that a programme of "marginal gains" needs to be adopted; however, this approach is also likely to be expensive, with no guarantee that each marginal gain will be additive.

The second question is, what is the "cut off" for a useful individual predication of outcome (or the cut off to move from the development of the algorithm to the external validation and impact assessment)? I have asserted here that the models presented fall below that cut off, and that it is likely patients would use any uncertainty in a poor outcome to justify higher expectations. Ultimately this decision would have to be based on an expectation of a demonstrable and cost-effective alteration in practice (with the difficulties intrinsic in defining and measuring this). I would argue that the presence of the optimism bias makes the importance of precise estimates even greater.

If a tool is developed that has individual discriminatory power that is considered sufficient to base predictions on, then several questions will require answering. Firstly, although I have investigated the effect a tool will have on expectations and decision, I have in no way attempted to quantify this relationship. It is also unclear how, or if, a poor prediction will affect outcome. An impact study, investigating these effects, would be required of any tool capable of individual risk prediction. Additionally, work examining different pathways for patients with different risks would be required. This could focus on modifying predictors of poor outcome (an approach that appeared to have some traction with patients in the qualitative work), or altering pathways towards alternative treatments for those with non-modifiable risk factors. A concern from patients was that this tool could be used to rationalise care, although others felt this was a reasonable approach.

Assuming a validated and useful prediction algorithm, the work that follows on from such an algorithm is complex. Quantifying the tool's effect on expectations, decision-making and outcome (both in terms of PROMs and health economics) would be required. Modifying risk factors to improve outcomes, along with altering pathways for patients with risk factors that cannot be modified, would require complex interventions to be assessed, likely as part of multiple RCTs.

8.2 Summary

In this thesis I have reviewed the epidemiology and treatment of knee OA, highlighting some of the issues with providing knee replacement services. The approach to help solve these issues has included:

- An examination of the factors affecting patient decision-making
- The development of a model of decision-making for patients considering a knee replacement
- An examination of how an outcome prediction tool could affect that decision-making
- The identification of factors that influence outcome in knee replacements
- The development of a study to quantify the relationship between pre-operative factors and outcome
- The conduct of a multicentre cohort study which produced a prognostic algorithm for patients considering a total knee replacement.

I have been successful in identifying important factors that influence patients' decision-making, and identifying that the optimism bias could affect any future outcome prediction tool. The multicentre cohort study was ultimately unable to offer clinically useful individualised predictions of outcomes; however, it is able to account for more of the variation in outcome than any previous report. This is certainly a step forward in the goal of individual outcome prediction.

Appendices

9.1 Appendix I: Focus group schedule

WELCOME

Thanks for agreeing to be part of the focus group. We appreciate your willingness to participate.

INTRODUCTIONS

Moderator; assistant moderator

"I will ask everyone to make their own introductions shortly, but before I do I want to cover some things."

PURPOSE OF FOCUS GROUPS

This focus group is aimed at understanding patients' views on decision-making for knee replacements. We need your input and want you to share your honest and open thoughts with us.

Before we start I would like to go through:

- Ground rules
- Plan for the afternoon

Ground Rules

1. WE WANT YOU TO DO THE TALKING.

We would like everyone to participate. I may call on you if I haven't heard from you in a while.

2. THERE ARE NO RIGHT OR WRONG ANSWERS

Every person's experiences and opinions are important. Please speak up whether you agree or disagree. We want to hear a wide range of opinions.

3. WHAT IS SAID IN THIS ROOM STAYS HERE

We want everyone to feel comfortable sharing when sensitive issues come up.

4. WE WILL BE TAPE RECORDING THE GROUP

We want to capture everything you have to say. We don't identify anyone by name in our report. You will remain anonymous.

Plan for the afternoon

I am shortly going to ask you all to complete a consent form. I will come round each of you in turn and ask you to sign it. While I am doing that I would like you to talk to the person next to you. I will then ask you to introduce them to the rest of the group.

PURPOSE OF FOCUS GROUP

This focus group is aimed at understanding how you made decisions about having a knee replacement and how a new tool, which we will explain fully later, might have influenced your decisions.

We would like to record the conversation. This recording will be used by the research team to ensure we don't miss anything. It will be transcribed (typed out) for us to analyse. We will ensure it is kept confidential at all times, and we will destroy the recording once the transcripts have been prepared. You will have the opportunity to look through the transcript and let us know if you would like to change anything.

We will combine this focus group with others, including some interviews. Some things you say may be used in a publication; however, we will make every effort to ensure you remain anonymous.

I expect this focus group to take around 1.5 to 2 hours. If, at any time, you feel tiered or want to stop please tell us.

HOW DID YOU GET HERE?

Can you tell us a little about yourself, and the events that lead to you to have a knee replacement please?

Prompts:

- How was the knee affecting your life?
- Is it difficult to cope with the knee?

- Were there things you could not do?
- Have you though about if it gets worse?
- What were the most important things that made you decide a knee replacement was for you?
- Do you think the problem with your knee is affected by the way you think, or the way you view the world? Try to elicit a sense of the patient's beliefs over the effect of psychological factors on outcome.
- Where did you go to get your information that helped you make a decision on your knee replacement? Why?
- How much information do you like? Why? (?? Fear)
- Where you afraid of anything to do with your treatment?
- What is the fear of – predominantly of the operation or of a poor outcome?
- Would this fear be affected by any delays to the operation (e.g. would a delay mean that you would feel more fear)?

Is there anything else you would like to say about decision-making in knee replacements?

Introduce OPT -- What is an outcome prediction tool

The outcome after knee replacement is variable – it is safe to say that almost all patients improve after a knee replacement; however, some patients improve more than others. We measure this improvement in various ways, but two of the most common are: function (i.e. how well the knee does things we want it to, like climbing stairs and getting into and out of a car – this is normally measured via questionnaires); the second is pain – some people have ongoing pain after a knee replacement.

Currently, we are not able to tell which patients will do very well from a functional point of view (up and down stairs, kneeling), and which patients will have ongoing pain. Patients who have ongoing pain tend to have worse function.

We are currently developing a questionnaire that may be able to predict outcome – i.e. it will be able to tell which patients are likely to develop pain and what functional improvement a patient can expect. This is what we mean by outcome prediction tool.

Do you have any questions?

What do you think of the outcome prediction tool?

I would like to start by going through a couple of examples of how an outcome prediction tool could look. I hope this will help you understand the type of information that will be included, and we would be interested in your views on how it is presented, and how easy it is to understand.

Prompts
- Do you find the charts helpful?
- Do you find identifying which patient you are helpful?
- Are rating things into categories a good idea?
- Do you understand the information – is there anything that could be improved?
- Is there too much information or too little?
- Is there too much detail or too little?

Do you think that having a prediction of the outcome would have been helpful to you?

Prompts
- Would you have trusted it?
- Would it have altered your decision (either way)?
- Would it have altered your expectations?
- Would it have affected your confidence or fear?
- Would it have given you more confidence to go ahead?
- If the outcome was good would you want an earlier TKR?
- If you had this information, would you have not gone to, for example, your family or friends, or a website. Why?

Does an OPT alter the fear of the procedure itself?

Who do you think should decide if you have a knee replacement?

Prompts:

- Should the surgeons decide?
- Should you have access to it whenever you like?

How would you have coped if you had a poor outcome? (Est time 10 min)

Prompts
- Suspicious?
- Not believe?
- Take it personally – would it feel like a personal attack?
- Would it feel like a diagnosis?
- Do you think it would help you cope after the operation?

Need to push here on the use of psychological factors. May need an explanation at this point, and an exploration of how they answer the above questions in the light of that.

Possibility of delaying Knee Replacement to modify other factors (e.g. CBT for coping strategies). What are your views on this?

Prompts

- Acceptable
- What if outcome is still poor
- Would you have been amenable to CBT or Motivational interviews or physio/increased physical exercise?

Who do you think should do the outcome prediction tool – the patient himself or herself, with the GP, a specialist nurse, or when they see the surgeon?

Is there anything else you would like to say about outcome prediction in knee replacements?

9.2 Appendix II: Interview schedule

WELCOME

Thanks for agreeing to take part. We appreciate your willingness to participate.

PURPOSE OF INTERVIEW

- This interview is aimed at understanding how you came to make a decision to go ahead with a knee replacement. We need your input and want you to share your honest and open thoughts with us. We would then like to understand how a new tool, which we will explain fully later, might have influenced your decisions.
- We would like to record the conversation. This recording will be used by the research team to ensure we don't miss anything. It will be transcribed (typed out) for us to analyse. We will ensure it is kept confidential at all times, and we will destroy the recording once the transcripts have been prepared. You will have the opportunity to look through the transcript and let us know if you would like to change anything.
- We will combine this interview with several other, including some focus groups. Some things you say may be used in a publication; however, we will make every effort to ensure you remain anonymous.
- I expect this interview to take around 30-40 minutes. If, at any time, you feel tiered or want to stop please tell us.

Personal situation and physical state

Can you tell us a little about yourself, and the events that lead to you being listed for a knee replacement please?

Prompts:

- How was the knee affecting your life?
- Is it difficult to cope with the knee?
- Were there things you could not do?
- Have you though about if it gets worse?
- What were the most important things that made you decide a knee replacement was for you?
- Do you think the problem with your knee is affected by the way you think, or the way you view the world? Try to elicit a sense of the patient's beliefs over the effect of psychological factors on outcome.

Sources of Information:

Where did you go to get your information that helped you make a decision on your knee replacement? Why?

Prompts:

- Friends family
- Website
- GP

How much information do you like? Why? (?? Fear)

The above are likely to be linked to consultation style preference – may need to discuss fear before discussing this, but if you get the opportunity it could be explored here.

Fear

Are you afraid of anything to do with your treatment?

What is the fear of – predominantly of the operation or of a poor outcome?

Would this fear be affected by any delays to the operation (e.g. would a delay mean that you would feel more fear)?

*Introduce OPT -- **What is an outcome prediction tool***

The outcome after knee replacement is variable – it is safe to say that almost all patients improve after a knee replacement; however, some patients improve more than others. We measure this improvement in various ways, but two of the most common are: function (i.e. how well the knee does things we want it to, like climbing stairs and getting into and out of a car – this is normally measured via questionnaires); the second is pain – some people have ongoing pain after a knee replacement.

Currently, we are not able to tell which patients will do very well from a functional point of view (up and down stairs, kneeling), and which patients will have ongoing pain. Patients who have ongoing pain tend to have worse function.

We are currently developing a questionnaire that will be able to predict outcome – i.e. it will be able to tell which patients are likely to develop pain and what functional improvement a patient can expect. This is what we mean by outcome prediction tool.

Does you have any questions?

What do you think of the outcome prediction tool?

I would like to start by going through a couple of examples of how an outcome prediction tool could look. I hope this will help you understand the type of information that will be included, and we would be interested in your views on how it is presented, and how easy it is to understand.

Prompts

- Do you find the charts helpful?
- Do you find identifying which patient you are helpful?
- Are rating things into categories a good idea?
- Do you understand the information – is there anything that could be improved?
- Is there too much information or too little?
- Is there too much detail or too little?

Do you think that having a prediction of the outcome would have been helpful to you?

Prompts

- Would you have trusted it?
- Would it have altered your decision (either way)?
- Would it have altered your expectations?
- Would it have affected your confidence or fear?
- Would it have given you more confidence to go ahead?
- If the outcome was good would you want an earlier TKR?
- If you had this information, would you have not gone to, for example, your family or friends, or a website. Why?
- **Make sure both good and bad outcomes are covered and get a sense for optimism bias**

Does an OPT alter the fear of the procedure itself?

Who do you think should decide if you have a knee replacement?

Prompts:

- Should the surgeons decide?
- Should you have access to it whenever you like?
- Do you think that things going on just now limit your ability to decide (e.g. struggling to do certain things with the knee (cope), fear of the operation).

How would you have coped if you had a poor outcome? (Est time 10 min)

Prompts
- Suspicious?
- Not believe?
- Take it personally – would it feel like a personal attack?
- Would it feel like a diagnosis?
- Do you think it would help you cope after the operation?

Need to push here on the use of psychological factors. May need an explanation at this point, and an exploration of how they answer the above questions in the light of that.

Possibility of delaying Knee Replacements to modify other factors (e.g. CBT for coping strategies). What are your views on this?

Prompts
- Acceptable
- What if outcome is still poor
- Would you have been amenable to CBT or Motivational interviews or physio/increased physical exercise.

Who do you think should do the outcome prediction tool – the patient himself or herself, with the GP, a specialist nurse, or when they see the surgeon?

Is there anything else you would like to say about outcome prediction in knee replacements?

9.3 Appendix III: Example of a fictitious outcome prediction tool

The Knee Outcome Report

Prepared for: Joe Bloggs

Date: 9/12/2013

Contents

The knee outcome report – what does it mean?

This report is designed to help you come to a decision regarding knee replacement surgery. If there is anything that you do not fully understand don't be afraid to ask.

You can discuss the outcome of this report with a health professional, who will be able to guide you through the information.

What is the aim of the report?

- To give an estimate of what you, as an individual, can expect from a knee replacement

What is in the report?

This report gives you an **estimate** on what you can expect from a knee replacement:

- It gives you the "bottom line" of what you can expect
- It gives a more detailed estimate on whether you will have any long term pain
- It gives a more detailed estimate of how well your knee will work (knee function) after a knee replacement

Different people will want different things from a knee replacement – for example one persons priority may be pain relief, while another may want to be able to walk to the shops.

Therefore, it is up to you to decide if the improvement that we have predicted is worthwhile for you.

How do you generate the report?

The report is generated through a detailed questionnaire that you have completed.

What do I do now?

We recommend that you discuss the report, and the pros and cons of an operation, with a healthcare provider. You will then be in a position to make an informed decision about a knee replacement.

2

The bottom line

One year after the operation:

There is a 30% chance you would not have had the operation if you could go back in time.

This means that if 100 people in your position had a knee replacement, 30 would not have the operation if they could go back in time

There is a 20% chance you would not recommend a knee replacement to a friend of member of your family.

This means that if 100 people in your position had a knee replacement, 20 would not recommend the treatment to a friend or member of their family.

There is a 15% chance you will still have pain in your knee after the operation.

This means that if 100 people in your position had a knee replacement, 15 would still have pain after the operation.

Your knee will work better after a knee replacement – this improvement is likely to be below average.

This means that most people in your position would improve more that you would. However, a small improvement may be very worthwhile to some patients, whereas a large improvement may not be worthwhile to another. It is up to you as an individual (with help from your surgeon) to decide if the operation is worthwhile.

Knee outcome report – Pain

Knee pain

Some patients have pain in their knee after they have had a knee replacement.

It is important to note that some patients may have a low chance of having pain and still develop it, and some patients may have a high chance and not develop pain.

Your chance of developing mild pain is 10%

This means that if 100 people in your category received a knee replacement, 10 would develop mild pain.

Your chance of developing moderate to severe pain is 5%

This means that is 100 people in your category received a knee replacement, 5 would develop moderate to severe pain.

THESE CHANCES ARE DEMONSTRATED IN THE DIAGRAM BELOW

 Patient without significant pain after knee replacement

 Patient with mild pain after knee replacement

 Patient with moderate to severe pain after knee replacement

Knee outcome report – Function

How your knee works (e.g. climbing stairs) ***before*** a knee replacement varies from person to person. Therefore, to get an idea of how much your knee may improve, you need to be able to know what it is like before an operation.

We have assed how your knee is works ***currently*** (before your knee replacement) using a scoring system. This is reported on a scale running from 1 (very poor function), to 100 (very good function). Your score is:

50

We expect your score (and therefore how well your knee works) to improve after a knee replacement. Some patients improve more than others.

Some patients find a small improvement in their score results in a **significant improvement in their quality of life. It is difficult to predict exactly how a knee replacement will affect you personally.**

We expect your score to improve by:

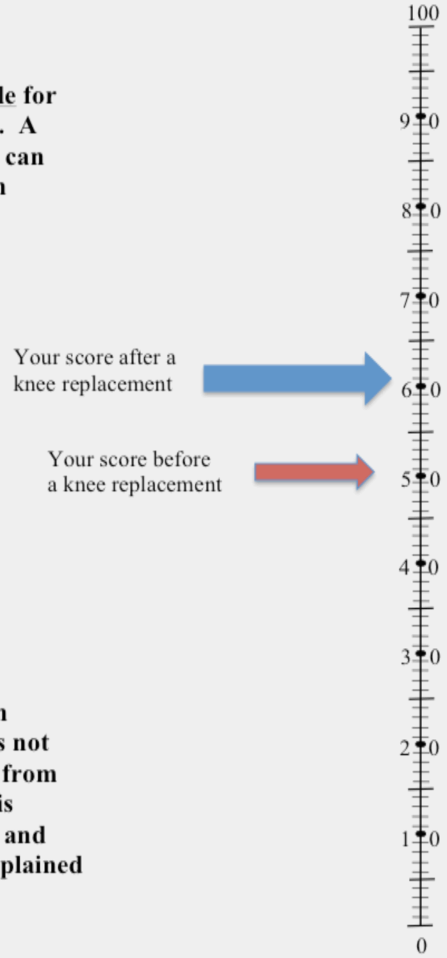
10 POINTS

What this means to you is explained in the following pages.

Best Possible knee function

We expect your knee function to improve by about 10 points. This is below average for a knee replacement.

A small improvement in knee function may be very worthwhile for one patient, but not for another. A small improvement on the scale can result in a large improvement in quality of life.



It is important to note that an improvement from 40 to 50 is not the same as an improvement from 50 to 60 – what is important is where you are starting from, and where you end up. This is explained in the following pages.

Worst Possible knee function

6

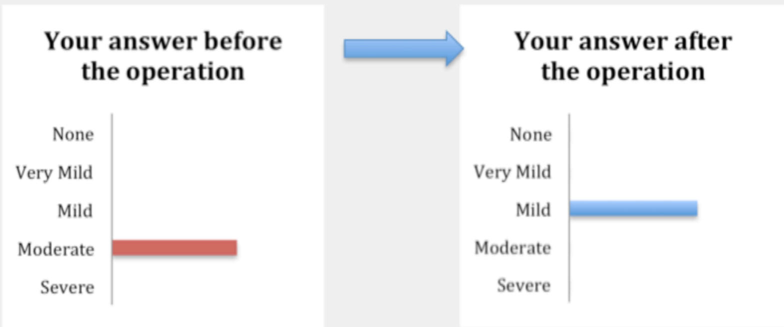
What does this mean for me?

To help understand what an improvement of 10 points could mean for you we have provided an example below.

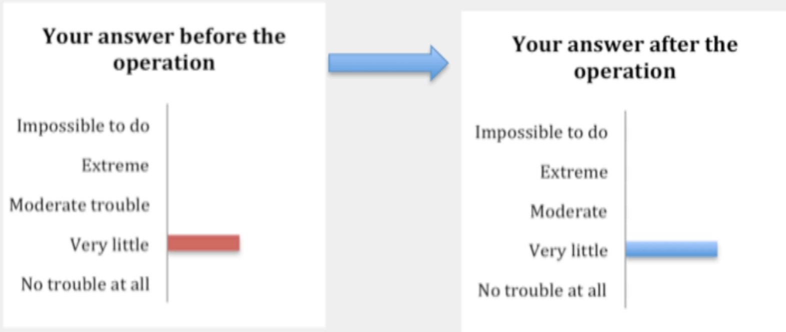
These are examples only. We are not able to predict each individual item, and you are likely to score higher, or lower, for several of them. However, the **overall** improvement is likely to be similar.

Each item below shows how you answer the question now, and how you are likely to answer it one year after the operation.

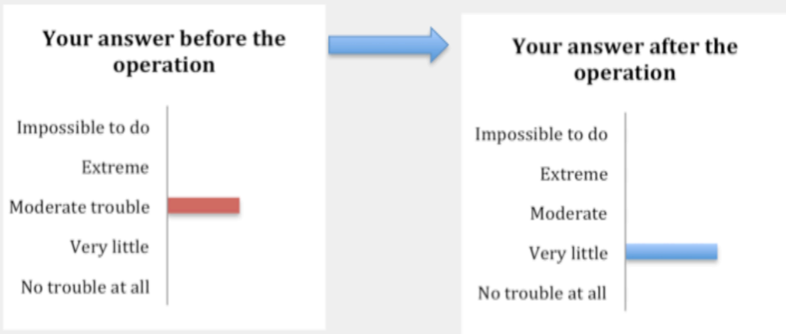
During the past 4 weeks, how would you describe the pain you usually have from your knee?



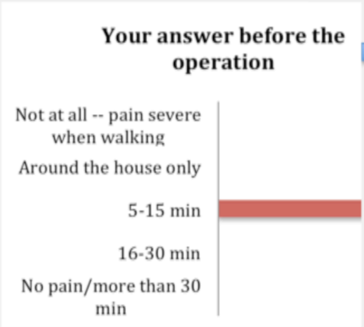
During the past 4 weeks, have you had any trouble with washing and drying yourself (all over) because of your knee?

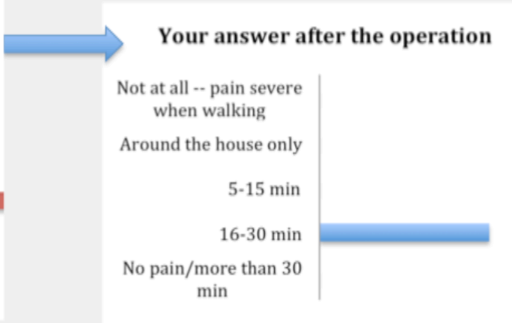


During the past 4 weeks, have you had any trouble getting in and out of a car or using public transport because of your knee?

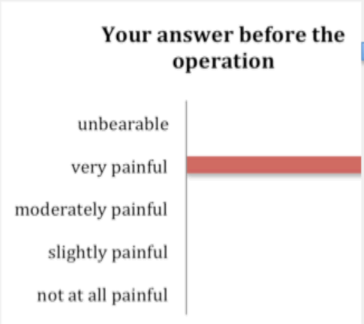


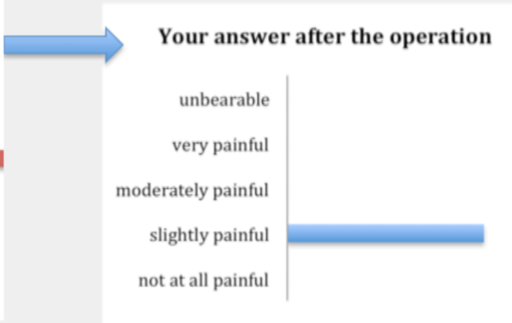
During the past 4 weeks, for how long have you been able to walk before pain from your knee becomes severe?





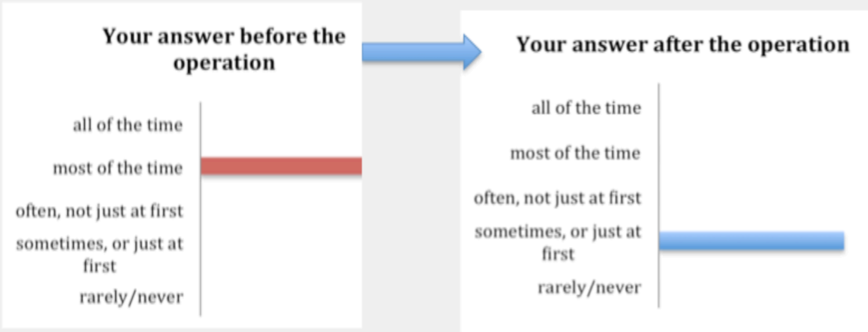
During the past 4 weeks, after a meal (sat at a table), how painful has it been for you to stand up from a chair because of your knee?



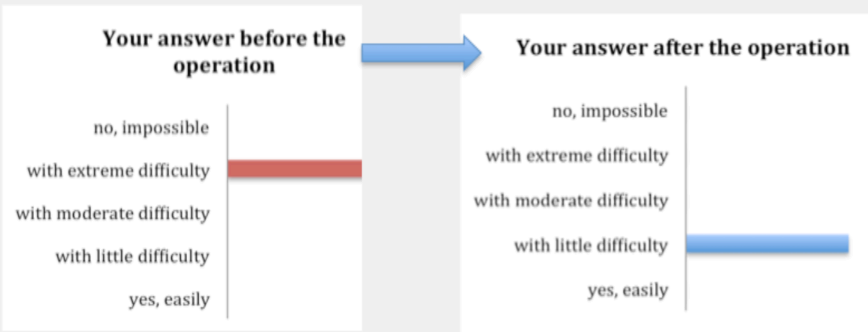


9

During the past 4 weeks, have you been limping when walking because of your knee?

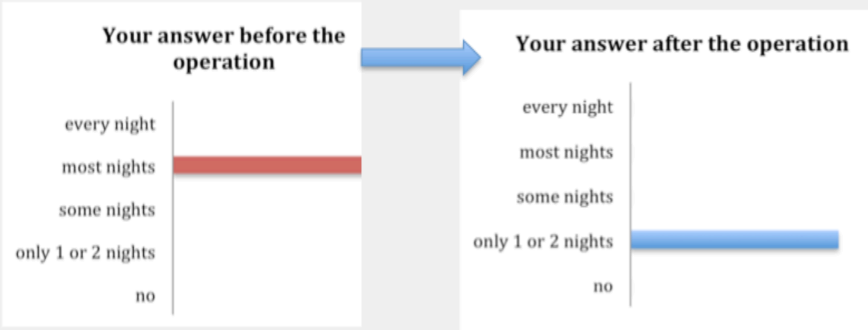


During the past 4 weeks, could you kneel down and get up again afterwards?

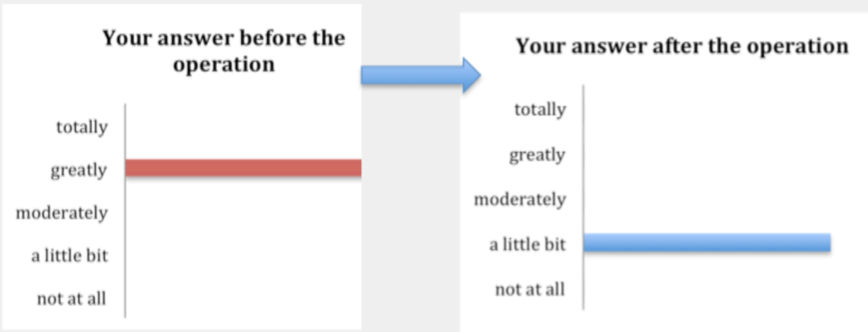


10

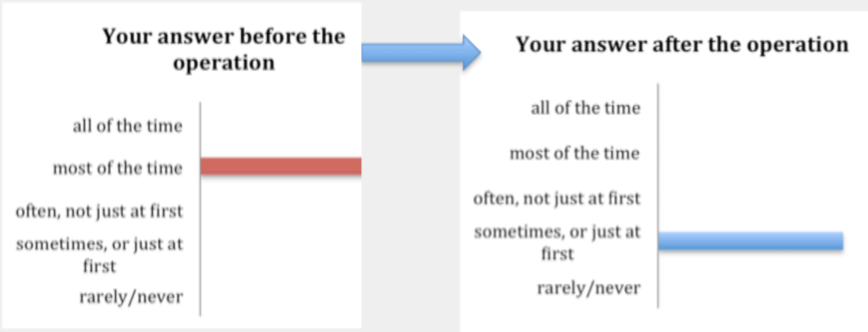
During the past 4 weeks, have you been troubled by pain from your knee in bed at night?



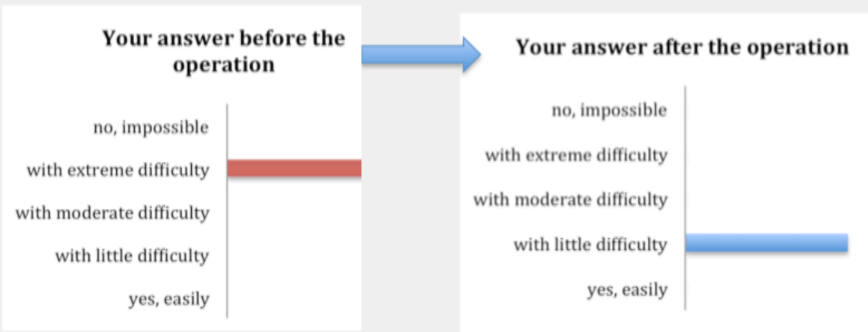
During the past 4 weeks, how much has pain from your knee interfered with your usual work (including housework)?



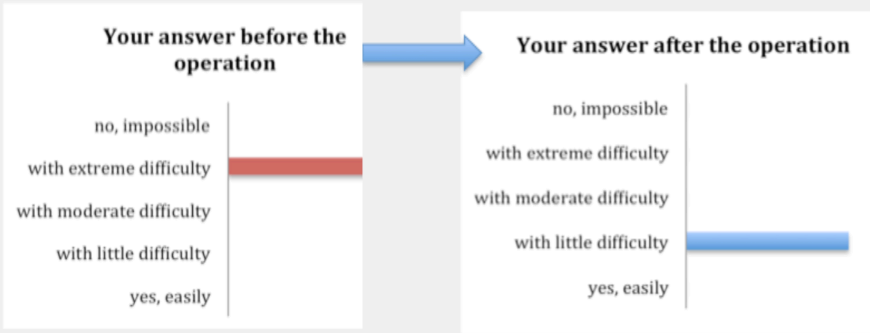
During the past 4 weeks, have you felt that your knee might suddenly "give way" or let you down?



During the past 4 weeks, could you do the household shopping on your own?



During the past 4 weeks, could you walk down one flight of stairs?

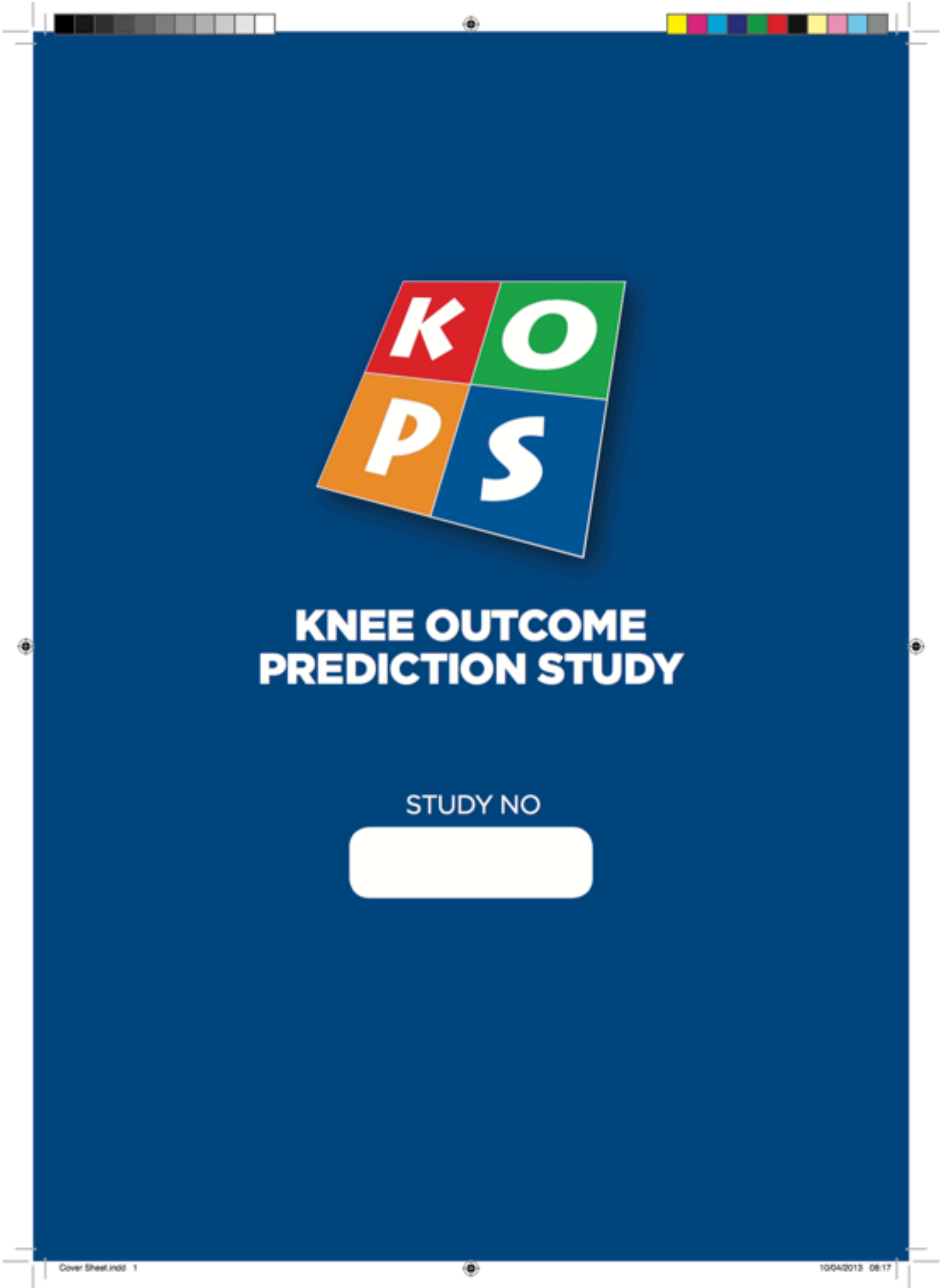


Should you have any questions or concerns regarding this report please discuss it with one of your healthcare providers.

9.4 Appendix IV: Search strategy – patient factors related to outcome

1. controlled.tw.
2. design.tw.
3. evidence.tw.
4. extraction.tw.
5. randomized controlled trials/
6. meta-analysis.tw.
7. review.tw.
8. sources.tw.
9. studies.tw.
10. or/1-9
11. letter.pt.
12. comment.pt.
13. editorial.pt.
14. or/11-13
15. 10 not 14
16. clinical trial.pt.
17. clinical trial, phase II.pt.
18. clinical trial, phase I.pt.
19. clinical trial, phase III.pt.
20. clinical trial, phase IV.pt.
21. controlled clinical trial.pt.
22. randomized controlled trial.pt.
23. or/16-22
24. 23 not 14
25. 15 or 24
26. cohort studies/
27. exp case-control studies/
28. exp cross-sectional studies/
29. or/25-28
30. arthroplasty, replacement, knee/
31. knee prosthesis/
32. exp arthroplasty/
33. joint prosthesis.mp.
34. exp "prostheses and implants"/
35. or/32-34
36. knee/
37. knee joint/
38. 36 or 37
39. 35 and 38
40. 30 or 31 or 39
41. 29 and 40
42. exp osteoarthritis/
43. 41 and 42

9.5 Appendix V: Questionnaires for KOPS



study number

Patient Information Form

Study Number:

NHS/Hospital Number:

Patient Name:

Address:

Postcode:

Phone Number:

Mobile Number:

Email Address:

Warwick Medical School

KNEE OUTCOME PREDICTION STUDY

study number

KOPS

form 03

Patient History

Sector [ ] NHS [ ] Private

Age [ ] years

Sex [ ] Male [ ] Female

Weight [ ] kg [ ] stone

Height [ ] m [ ] feet [ ] inches

Do you live alone? [ ] yes [ ] no

Occupation *(tick one)*

Main occupation during working life [ ]

[ ] Heavy manual *e.g. construction worker/miner*

[ ] Moderate manual *e.g. cleaner/plumber*

[ ] Light manual *e.g. driver/salesperson/housewife*

[ ] Sedentary *e.g. writer/receptionist*

Knee being operated on [ ] left [ ] right

Have you had a knee replacement on your other knee? [ ] yes [ ] no

Onset of disease [ ] years ago

Treatment *(tick all that apply)*

[ ] Simple analgesia *e.g. Paracetemol/Co-codamol*

[ ] Anti-inflammatories *e.g. NSAIDs*

[ ] Walking aids

[ ] Physiotherapy

[ ] Arthroscopy *(diagnostic or therapeutic)*

[ ] Dietary supplements *e.g. glucosamine*

[ ] Alternative medicine *e.g. acupuncture*

V5.1 | Apr 13

Warwick Medical School

Oxford Knee Score

Instructions Please answer every question. Some questions may look like others, but each one is different. Please take the time to read and answer each question carefully by putting a tick in the box that best represents your response.

Example

Q01 During the past 4 weeks, how would you describe the pain you have from your knee?

none	very mild	mild	moderate	severe
[ ]	[ ]	[ ]	[✓]	[ ]

Please begin answering the questions now.

Problems with your knee

Q01 During the past 4 weeks, how would you describe the pain you **usually** have from your knee?

none	very mild	mild	moderate	severe
[ ]	[ ]	[ ]	[ ]	[ ]

Q02 During the past 4 weeks, have you had any trouble with washing and drying yourself (all over) **because of your knee**?

no trouble at all	very little trouble	moderate trouble	Extreme difficulty	impossible to do
[ ]	[ ]	[ ]	[ ]	[ ]

Q03 During the past 4 weeks, have you had any trouble getting in and out of a car or using public transport **because of you knee**? *(whichever you would tend to use)*

no trouble at all	very little trouble	moderate trouble	Extreme difficulty	impossible to do
[ ]	[ ]	[ ]	[ ]	[ ]

Q04 During the past four weeks, for how long have you been able to walk before **pain from your knee** becomes **severe**? *(with or without a stick)*

No pain/more than 30 mins	16-30 mins	5-15 mins	around the house only	not at all – pain severe when walking
[ ]	[ ]	[ ]	[ ]	[ ]

Q05 During the past 4 weeks, after a meal (sat at a table), how painful has it been for you to stand up from a chair **because of your knee**?

not at all painful	slightly painful	moderately painful	very painful	unbearable
[ ]	[ ]	[ ]	[ ]	[ ]

PTO

Q06 During the past 4 weeks, have you been limping when walking **because of your knee**?

rarely/never	sometimes, or just at first	often, not just at first	most of the time	all of the time
[ ]	[ ]	[ ]	[ ]	[ ]

Q07 During the past 4 weeks, could you kneel down and get up again afterwards?

yes, easily	with little difficulty	with moderate difficulty	with extreme difficulty	no, impossible
[ ]	[ ]	[ ]	[ ]	[ ]

Q08 During the past 4 weeks, have you been troubled by **pain from your knee** in bed at night?

No	Only 1 or 2 nights	Some nights	Most nights	Every night
[ ]	[ ]	[ ]	[ ]	[ ]

Q09 During the past 4 weeks, how much has **pain from your knee** interfered with your usual work (including housework)?

Not at all	A little bit	Moderately	Greatly	Totally
[ ]	[ ]	[ ]	[ ]	[ ]

Q10 During the past 4 weeks, have you felt that your knee might suddenly 'give way' or let you down?

rarely/never	sometimes, or just at first	often, not just at first	most of the time	all of the time
[ ]	[ ]	[ ]	[ ]	[ ]

Q11 During the past 4 weeks, **could** you do the household shopping **on your own**?

yes, easily	with little difficulty	with moderate difficulty	with extreme difficulty	no, impossible
[ ]	[ ]	[ ]	[ ]	[ ]

Q12 During the past 4 weeks, **could** you walk down one flight of stairs?

yes, easily	with little difficulty	with moderate difficulty	with extreme difficulty	no, impossible
[ ]	[ ]	[ ]	[ ]	[ ]

KNEE OUTCOME PREDICTION STUDY

study number

KOPS

form 05

General Health

Instructions

Example

Q01 How strongly do you disagree with the following statements?

	all of the time	most of the time	some of the time	a little of the time	none of the time
a. did you feel full of life?	[ ]	[ ]	[✓]	[ ]	[ ]
b. have you been very nervous?	[ ]	[✓]	[ ]	[ ]	[ ]

Please begin answering the questions now.

Q01 In general, would you say your health is:

excellent	very good	good	fair	poor
[ ]	[ ]	[ ]	[ ]	[ ]

Q02 **Compared to one year ago**, how would you rate your health in general **now**?

much better now than one year ago	somewhat better now than one year ago	about the same as one year ago	somewhat worse now than one year ago	much worse than one year ago
[ ]	[ ]	[ ]	[ ]	[ ]

Q03 The following questions are about activities you might do during a typical day. Does your health **now** limit you in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a. **vigorous activities** such as running, lifting heavy objects, participating in strenuous sports	[ ]	[ ]	[ ]
b. **moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling or playing golf	[ ]	[ ]	[ ]
c. **lifting or carrying groceries**	[ ]	[ ]	[ ]
d. climbing **several** flights of stairs	[ ]	[ ]	[ ]
e. climbing **one** flight of stairs	[ ]	[ ]	[ ]
f. bending, kneeling or stooping	[ ]	[ ]	[ ]
g. walking **more than a mile**	[ ]	[ ]	[ ]
h. walking **several hundred yards**	[ ]	[ ]	[ ]
i. walking **one hundred yards**	[ ]	[ ]	[ ]
j. bathing or dressing yourself	[ ]	[ ]	[ ]

PTO

Q04 During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**?

	all of the time	most of the time	some of the time	a little of the time	none of the time
a. cut down on the **amount of time** you spent on work or other activities	[ ]	[ ]	[ ]	[ ]	[ ]
b. **accomplished less** than you would like	[ ]	[ ]	[ ]	[ ]	[ ]
c. were **limited** in the **kind** of work or other activities	[ ]	[ ]	[ ]	[ ]	[ ]
d. had **difficulty** performing the work or other activities *(eg. it took extra effort)*	[ ]	[ ]	[ ]	[ ]	[ ]

Q05 **During the past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

	all of the time	most of the time	some of the time	a little of the time	none of the time
a. cut down on the **amount of time** you spent on work or other activities	[ ]	[ ]	[ ]	[ ]	[ ]
b. **accomplished less** than you would like	[ ]	[ ]	[ ]	[ ]	[ ]
c. did work or other activities less **carefully** than usual	[ ]	[ ]	[ ]	[ ]	[ ]

Q06 During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours or groups?

not at all	slightly	moderately	quite a bit	extremely
[ ]	[ ]	[ ]	[ ]	[ ]

Q07 How much physical pain have you had **during the past 4 weeks**?

none	very mild	mild	moderate	severe	very severe
[ ]	[ ]	[ ]	[ ]	[ ]	[ ]

Q08 During the **past 4 weeks**, how much did **pain** interfere with your normal work?
(including both work outside the home and housework)

not at all	slightly	moderately	quite a bit	extremely
[ ]	[ ]	[ ]	[ ]	[ ]

Q09 These questions are about how you feel and how things have been with you **during the past 4 weeks**. Please give the one answer that is closest to the way you have been feeling for each item. How much time during the **past 4 weeks**...

	all of the time	most of the time	some of the time	a little of the time	none of the time
a. did you feel full of life?	[ ]	[ ]	[ ]	[ ]	[ ]
b. have you been very nervous?	[ ]	[ ]	[ ]	[ ]	[ ]
c. have you felt so down in the dumps that nothing could cheer you up?	[ ]	[ ]	[ ]	[ ]	[ ]
d. have you felt calm and peaceful?	[ ]	[ ]	[ ]	[ ]	[ ]
e. did you have a lot of energy?	[ ]	[ ]	[ ]	[ ]	[ ]
f. have you felt depressed?	[ ]	[ ]	[ ]	[ ]	[ ]
g. did you feel worn out?	[ ]	[ ]	[ ]	[ ]	[ ]
h. have you been happy?	[ ]	[ ]	[ ]	[ ]	[ ]
i. did you feel tired?	[ ]	[ ]	[ ]	[ ]	[ ]

Q10 During the past 4 weeks, how much of the time has your **physical health or emotional problems** interfered with your social activities? *(like visiting with friends, relatives, etc.)*

all of the time	most of the time	some of the time	a little of the time	none of the time
[ ]	[ ]	[ ]	[ ]	[ ]

Q11 How TRUE or FALSE is **each** of the following statements for you?

	definitely true	mostly true	don't know	mostly false	definitely false
a. I seem to get sick a little easier than other people	[ ]	[ ]	[ ]	[ ]	[ ]
b. I am as healthy as anybody I know	[ ]	[ ]	[ ]	[ ]	[ ]
c. I expect my health to get worse	[ ]	[ ]	[ ]	[ ]	[ ]
d. my health is excellent	[ ]	[ ]	[ ]	[ ]	[ ]

KNEE OUTCOME PREDICTION STUDY

study number

form 06

Medical Comorbidity

The following is a list of common problems. Please indicate if you currently have the problem in the first column. If you do not have the problem, move on to the next problem. If you do have the problem, please indicate in the second column if you receive medications or some other type of treatment for the problem. In the third column, please indicate if the problem limits any of your activities. Finally, please indicate under 'other medical problems' at the foot of the page all medical conditions that are not listed.

	Do you have the problem?	Do you receive treatment for it?	Does it limit your activities
Heart disease	[YES] [NO]	[YES] [NO]	[YES] [NO]
High blood pressure	[YES] [NO]	[YES] [NO]	[YES] [NO]
Lung disease	[YES] [NO]	[YES] [NO]	[YES] [NO]
Diabetes	[YES] [NO]	[YES] [NO]	[YES] [NO]
Ulcer or stomach disease	[YES] [NO]	[YES] [NO]	[YES] [NO]
Kidney disease	[YES] [NO]	[YES] [NO]	[YES] [NO]
Liver disease	[YES] [NO]	[YES] [NO]	[YES] [NO]
Anaemia or other blood disorder	[YES] [NO]	[YES] [NO]	[YES] [NO]
Cancer	[YES] [NO]	[YES] [NO]	[YES] [NO]
Depression	[YES] [NO]	[YES] [NO]	[YES] [NO]
Osteoarthritis or degenerative arthritis	[YES] [NO]	[YES] [NO]	[YES] [NO]
Back pain	[YES] [NO]	[YES] [NO]	[YES] [NO]
Rheumatoid arthritis	[YES] [NO]	[YES] [NO]	[YES] [NO]

Other medical problems *(please write down the condition)*

	[YES] [NO]	[YES] [NO]	[YES] [NO]
	[YES] [NO]	[YES] [NO]	[YES] [NO]
	[YES] [NO]	[YES] [NO]	[YES] [NO]

FOR RESEARCHERS ONLY

Charlston Score [ ]

V5.3 | Oct 13

Warwick Medical School

[06] Medical Comorbidity.indd 1

25/10/2013 09:12

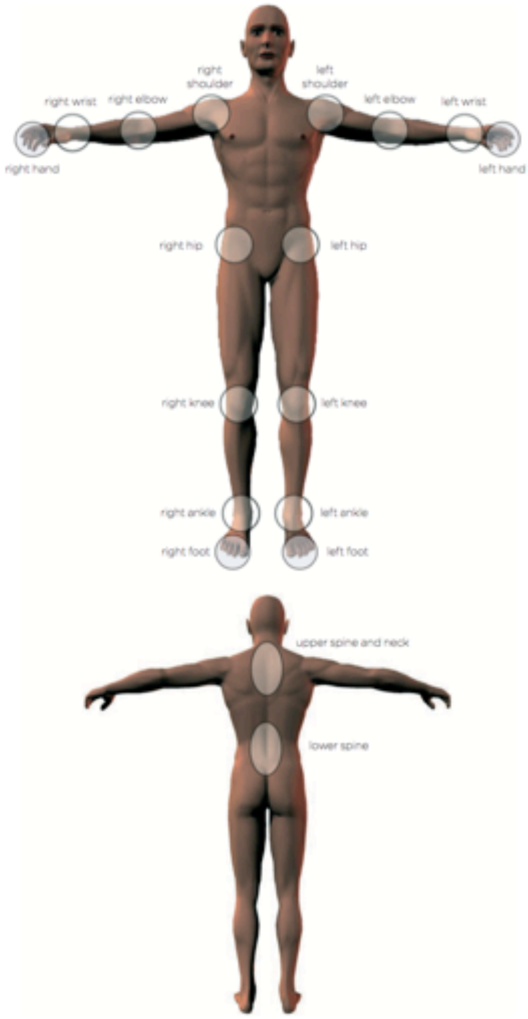
KNEE OUTCOME PREDICTION STUDY

study number

form 07

Joint Comorbidity

Please indicate which joints have caused you noticeable problems during the **last week**.
Place a tick in as many of the circles that apply *(including the knee on which we are going to operate)*.



V5.0 | Jan 13

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[07] Joint Comorbidity.indd 1 18/02/2013 11:19

Arthritis Helplessness Index

Please answer every question. Please take the time to read each statement carefully and put a tick in the box that best represents your response.

Q01 Arthritis is controlling my life.

strongly agree	agree	disagree	strongly disagree
[ ]	[ ]	[ ]	[ ]

Q02 Managing my arthritis is largely my own responsibility.

strongly agree	agree	disagree	strongly disagree
[ ]	[ ]	[ ]	[ ]

Q03 I can reduce my pain by staying calm and relaxed.

strongly agree	agree	disagree	strongly disagree
[ ]	[ ]	[ ]	[ ]

Q04 Too often, my pain just seems to hit me from out of the blue.

strongly agree	agree	disagree	strongly disagree
[ ]	[ ]	[ ]	[ ]

Q05 If I do all the right things, I can successfully manage my arthritis.

strongly agree	agree	disagree	strongly disagree
[ ]	[ ]	[ ]	[ ]

Q06 I can do a lot of things myself to cope with my arthritis.

strongly agree	agree	disagree	strongly disagree
[ ]	[ ]	[ ]	[ ]

Q07 When it comes to manageing my arthritis, I feel I can only do what my doctor tells me to do.

strongly agree	agree	disagree	strongly disagree
[ ]	[ ]	[ ]	[ ]

Q08 When I manage my personal life well, my arthritis does not flare as much.

strongly agree	agree	disagree	strongly disagree
[ ]	[ ]	[ ]	[ ]

Q09 I have considerable ability to control my pain.

strongly agree	agree	disagree	strongly disagree
[ ]	[ ]	[ ]	[ ]

PTO

Q10 I would feel helpless if I couldn't rely on other people for help with my arthritis.

strongly agree	agree	disagree	strongly disagree
[ ]	[ ]	[ ]	[ ]

Q11 Usually, I can tell when my arthritis will flare.

strongly agree	agree	disagree	strongly disagree
[ ]	[ ]	[ ]	[ ]

Q12 No matter what I do or how hard I try, I just can't seem to get relief from my pain.

strongly agree	agree	disagree	strongly disagree
[ ]	[ ]	[ ]	[ ]

Q13 I am coping effectively with my arthritis.

strongly agree	agree	disagree	strongly disagree
[ ]	[ ]	[ ]	[ ]

Q14 It seems as though fate and other factors beyond my control affect my arthritis.

strongly agree	agree	disagree	strongly disagree
[ ]	[ ]	[ ]	[ ]

Q15 I want to learn as much as I can about arthritis.

strongly agree	agree	disagree	strongly disagree
[ ]	[ ]	[ ]	[ ]

Expectation After Surgery

The answers that you give in this questionnaire are confidential. All information will remain anonymised and your surgeon will not be able to connect your name to this information.

Example

Q01 After one year, how much pain do you expect you will have in your knee?

none	very mild	mild	moderate	severe
[ ]	[✓]	[ ]	[ ]	[ ]

HOW IMPORTANT IS THIS TO YOU?
- [ ] extremely important
- [✓] very important
- [ ] moderately important
- [ ] slightly important
- [ ] not at all important

Please begin answering the questions now.

Q01 Have you spoken to your surgeon about your operation today? [ ] yes [ ] no

Q02 Do you know anyone else who has had knee replacement surgery?
[ ] yes [ ] no

Q03 If yes, was it your impression that they were generally pleased with the results of their knee surgery or not?

generally pleased	generally not pleased	mixed	don't know
[ ]	[ ]	[ ]	[ ]

Imagine you are answering the next questions one year after your knee surgery. What would you **realistically** expect your answers to be?

Q04 After one year, how much pain do you expect you will have in your knee?

none	very mild	mild	moderate	severe
[ ]	[ ]	[ ]	[ ]	[ ]

HOW IMPORTANT IS THIS TO YOU?
- [ ] extremely important
- [ ] very important
- [ ] moderately important
- [ ] slightly important
- [ ] not at all important

Q05 After one year, do you expect you will have trouble with washing and drying yourself (all over) **because of your knee**?

no trouble at all	very little trouble	moderate trouble	extreme difficulty	impossible to do
[ ]	[ ]	[ ]	[ ]	[ ]

HOW IMPORTANT IS THIS TO YOU?
- [ ] extremely important
- [ ] very important
- [ ] moderately important
- [ ] slightly important
- [ ] not at all important

PTO

Q06 After one year, do you expect you will have trouble getting in and out of your car or using public transport **because of your knee**? *(whichever you would tend to use)*

no trouble at all	very little trouble	moderate trouble	extreme difficulty	impossible to do
[ ]	[ ]	[ ]	[ ]	[ ]

HOW IMPORTANT IS THIS TO YOU?
- [ ] extremely important
- [ ] very important
- [ ] moderately important
- [ ] slightly important
- [ ] not at all important

Q07 After one year, for how long do you expect you will be able to walk before **pain from your knee** becomes severe? *(with or without a stick)*

no pain/more than 30 mins	16-30 mins	5-15 mins	around the house only	not at all - pain severe when walking
[ ]	[ ]	[ ]	[ ]	[ ]

HOW IMPORTANT IS THIS TO YOU?
- [ ] extremely important
- [ ] very important
- [ ] moderately important
- [ ] slightly important
- [ ] not at all important

Q08 After one year, when sitting at a table after a meal, how painful will it be for you to stand up from a chair **because of your knee**?

not at all painful	slightly painful	moderately painful	very painful	all of the time
[ ]	[ ]	[ ]	[ ]	[ ]

HOW IMPORTANT IS THIS TO YOU?
- [ ] extremely important
- [ ] very important
- [ ] moderately important
- [ ] slightly important
- [ ] not at all important

Q09 After one year, do you expect you will be limping when walking **because of your knee**?

rarely/never	sometimes/just at first	often, not just at first	most of the time	all of the time
[ ]	[ ]	[ ]	[ ]	[ ]

HOW IMPORTANT IS THIS TO YOU?
- [ ] extremely important
- [ ] very important
- [ ] moderately important
- [ ] slightly important
- [ ] not at all important

Q10 After one year, do you expect you could kneel down and get up again afterwards?

yes, easily	with little difficulty	with moderate difficulty	with extreme difficulty	no, impossible
[ ]	[ ]	[ ]	[ ]	[ ]

HOW IMPORTANT IS THIS TO YOU?
- [ ] extremely important
- [ ] very important
- [ ] moderately important
- [ ] slightly important
- [ ] not at all important

Q11 After one year, do you expect you will be troubled by **pain from your knee** in bed at night?

never	rarely	some nights	most nights	every night
[ ]	[ ]	[ ]	[ ]	[ ]

HOW IMPORTANT IS THIS TO YOU?
- [ ] extremely important
- [ ] very important
- [ ] moderately important
- [ ] slightly important
- [ ] not at all important

Q12 After one year, do you expect the **pain from your knee** will interfere with your usual work? *(including housework)*

rarely/never	sometimes/just at first	often, not just at first	most of the time	all of the time
[ ]	[ ]	[ ]	[ ]	[ ]

HOW IMPORTANT IS THIS TO YOU?
- [ ] extremely important
- [ ] very important
- [ ] moderately important
- [ ] slightly important
- [ ] not at all important

Q13 After one year, do you expect your knee will 'give way' or let you down?

rarely/never	sometimes/just at first	often, not just at first	most of the time	all of the time
[ ]	[ ]	[ ]	[ ]	[ ]

HOW IMPORTANT IS THIS TO YOU?
[ ] extremely important
[ ] very important
[ ] moderately important
[ ] slightly important
[ ] not at all important

Q14 After one year, do you expect you will be able to go household shopping **on your own**?

yes, easily	with little difficulty	with moderate difficulty	with extreme difficulty	no, impossible
[ ]	[ ]	[ ]	[ ]	[ ]

HOW IMPORTANT IS THIS TO YOU?
[ ] extremely important
[ ] very important
[ ] moderately important
[ ] slightly important
[ ] not at all important

Q15 After one year, do you expect you will be able to walk down one flight of stairs?

yes, easily	with little difficulty	with moderate difficulty	with extreme difficulty	no, impossible
[ ]	[ ]	[ ]	[ ]	[ ]

HOW IMPORTANT IS THIS TO YOU?
[ ] extremely important
[ ] very important
[ ] moderately important
[ ] slightly important
[ ] not at all important

Hospital Anxiety & Depression Scale

Doctors are aware that emotions play an important part in most illnesses. If your doctor knows about these feelings, he or she will be able to help you more. This questionnaire is designed to help your doctor know how you feel. Read each item and place a firm tick in the box opposite the reply which comes closest to **how you have been feeling in the past week**. Don't take too long over your replies; your immediate reaction to each item will probably be more accurate than a long thought out response.

Q01 I feel tense or 'wound up'...

most of the time	a lot of the time	time to time, occasionally	not at all
[ ]	[ ]	[ ]	[ ]

Q02 I still enjoy the things I used to enjoy...

definitely as much	not quite so much	only a little	not at all
[ ]	[ ]	[ ]	[ ]

Q03 I get a sort of frightened feeling like something awful is about to happen...

very definitely and quite badly	yes, but not too badly	a little, but it doesn't worry me	not at all
[ ]	[ ]	[ ]	[ ]

Q04 I can laugh and see the funny side of things...

as much as I always could	not quite so much now	definitely not so much now	not at all
[ ]	[ ]	[ ]	[ ]

Q05 Worrying thoughts go through my mind...

a great deal of the time	a lot of the time	from time to time, but not too often	only occasionally
[ ]	[ ]	[ ]	[ ]

Q06 I feel cheerful...

not at all	not often	sometimes	most of the time
[ ]	[ ]	[ ]	[ ]

Q07 I can sit at ease and feel relaxed...

definitely	usually	not often	not at all
[ ]	[ ]	[ ]	[ ]

Q08 I feel as if I am slowed down...

nearly all of the time	very often	sometimes	not at all
[ ]	[ ]	[ ]	[ ]

PTO

KNEE OUTCOME PREDICTION STUDY

KOPS

form 10 P2

Q09	I get a sort of frightened feeling like 'butterflies in the stomach'...			
	not at all [ ]	occasionally [ ]	quite often [ ]	very often [ ]
Q10	I have lost interest in my appearance...			
	definitely [ ]	I don't take as much care as I should [ ]	I may not take quite as much care [ ]	I take just as much care as ever [ ]
Q11	I feel restless, as if I have to be on the move...			
	very much indeed [ ]	quite a lot [ ]	not very much [ ]	not at all [ ]
Q12	I look forward with enjoyment to things...			
	as much as I ever did [ ]	rather less than I used to [ ]	definitely less than I used to [ ]	hardly at all [ ]
Q13	I get sudden feelings of panic...			
	very often indeed [ ]	quite often [ ]	not very often [ ]	not at all [ ]
Q14	I can enjoy a good book or radio or TV programme...			
	often [ ]	sometimes [ ]	not often [ ]	very seldom [ ]

Thank you for completing the questionnaire.

6 Month Oxford Knee Score

Instructions Please answer every question. Some questions may look like others, but each one is different. Please take the time to read and answer each question carefully by putting a tick in the box that best represents your response.

Example

Q01 During the past 4 weeks, how would you describe the pain you have from your knee?

none	very mild	mild	moderate	severe
[ ]	[ ]	[ ]	[ ]	[ ]

Please begin answering the questions now.

Problems with your knee

Q01 During the past 4 weeks, how would you describe the pain you **usually** have from your knee?

none	very mild	mild	moderate	severe
[ ]	[ ]	[ ]	[ ]	[ ]

Q02 During the past 4 weeks, have you had any trouble with washing and drying yourself (all over) **because of your knee**?

no trouble at all	very little trouble	moderate trouble	Extreme difficulty	impossible to do
[ ]	[ ]	[ ]	[ ]	[ ]

Q03 During the past 4 weeks, have you had any trouble getting in and out of a car or using public transport **because of you knee**? *(whichever you would tend to use)*

no trouble at all	very little trouble	moderate trouble	Extreme difficulty	impossible to do
[ ]	[ ]	[ ]	[ ]	[ ]

Q04 During the past four weeks, for how long have you been able to walk before **pain from your knee** becomes **severe**? *(with or without a stick)*

No pain/more than 30 mins	16-30 mins	5-15 mins	around the house only	not at all — pain severe when walking
[ ]	[ ]	[ ]	[ ]	[ ]

Q05 During the past 4 weeks, after a meal (sat at a table), how painful has it been for you to stand up from a chair **because of your knee**?

not at all painful	slightly painful	moderately painful	very painful	unbearable
[ ]	[ ]	[ ]	[ ]	[ ]

PTO

Q06 During the past 4 weeks, have you been limping when walking **because of your knee**?

rarely/never	sometimes, or just at first	often, not just at first	most of the time	all of the time
[ ]	[ ]	[ ]	[ ]	[ ]

Q07 During the past 4 weeks, could you kneel down and get up again afterwards?

yes, easily	with little difficulty	with moderate difficulty	with extreme difficulty	no, impossible
[ ]	[ ]	[ ]	[ ]	[ ]

Q08 During the past 4 weeks, have you been troubled by **pain from your knee** in bed at night?

No	Only 1 or 2 nights	Some nights	Most nights	Every night
[ ]	[ ]	[ ]	[ ]	[ ]

Q09 During the past 4 weeks, how much has **pain from your knee** interfered with your usual work (including housework)?

Not at all	A little bit	Moderately	Greatly	Totally
[ ]	[ ]	[ ]	[ ]	[ ]

Q10 During the past 4 weeks, have you felt that your knee might suddenly 'give way' or let you down?

rarely/never	sometimes, or just at first	often, not just at first	most of the time	all of the time
[ ]	[ ]	[ ]	[ ]	[ ]

Q11 During the past 4 weeks, **could** you do the household shopping **on your own**?

yes, easily	with little difficulty	with moderate difficulty	with extreme difficulty	no, impossible
[ ]	[ ]	[ ]	[ ]	[ ]

Q12 During the past 4 weeks, **could** you walk down one flight of stairs?

yes, easily	with little difficulty	with moderate difficulty	with extreme difficulty	no, impossible
[ ]	[ ]	[ ]	[ ]	[ ]

Thank you for completing the questionnaire.

KNEE OUTCOME PREDICTION STUDY

study number

KOPS

form 15

12 Month Oxford Knee Score

Instructions Please answer every question. Some questions may look like others, but each one is different. Please take the time to read and answer each question carefully by putting a tick in the box that best represents your response.

Example

Q01 During the past 4 weeks, how would you describe the pain you have from your knee?

none	very mild	mild	moderate	severe
[ ]	[ ]	[ ]	[ ]	[ ]

Please begin answering the questions now.

Problems with your knee

Q01 During the past 4 weeks, how would you describe the pain you **usually** have from your knee?

none	very mild	mild	moderate	severe
[ ]	[ ]	[ ]	[ ]	[ ]

Q02 During the past 4 weeks, have you had any trouble with washing and drying yourself (all over) **because of your knee**?

no trouble at all	very little trouble	moderate trouble	Extreme difficulty	impossible to do
[ ]	[ ]	[ ]	[ ]	[ ]

Q03 During the past 4 weeks, have you had any trouble getting in and out of a car or using public transport **because of you knee**? *(whichever you would tend to use)*

no trouble at all	very little trouble	moderate trouble	Extreme difficulty	impossible to do
[ ]	[ ]	[ ]	[ ]	[ ]

Q04 During the past four weeks, for how long have you been able to walk before **pain from your knee** becomes **severe**? *(with or without a stick)*

No pain/more than 30 mins	16-30 mins	5-15 mins	around the house only	not at all – pain severe when walking
[ ]	[ ]	[ ]	[ ]	[ ]

Q05 During the past 4 weeks, after a meal (sat at a table), how painful has it been for you to stand up from a chair **because of your knee**?

not at all painful	slightly painful	moderately painful	very painful	unbearable
[ ]	[ ]	[ ]	[ ]	[ ]

PTO

V5.0 | Jan 13

Warwick Medical School

Q06 During the past 4 weeks, have you been limping when walking **because of your knee**?

rarely/never	sometimes, or just at first	often, not just at first	most of the time	all of the time
[ ]	[ ]	[ ]	[ ]	[ ]

Q07 During the past 4 weeks, could you kneel down and get up again afterwards?

yes, easily	with little difficulty	with moderate difficulty	with extreme difficulty	no, impossible
[ ]	[ ]	[ ]	[ ]	[ ]

Q08 During the past 4 weeks, have you been troubled by **pain from your knee** in bed at night?

No	Only 1 or 2 nights	Some nights	Most nights	Every night
[ ]	[ ]	[ ]	[ ]	[ ]

Q09 During the past 4 weeks, how much has **pain from your knee** interfered with your usual work (including housework)?

Not at all	A little bit	Moderately	Greatly	Totally
[ ]	[ ]	[ ]	[ ]	[ ]

Q10 During the past 4 weeks, have you felt that your knee might suddenly 'give way' or let you down?

rarely/never	sometimes, or just at first	often, not just at first	most of the time	all of the time
[ ]	[ ]	[ ]	[ ]	[ ]

Q11 During the past 4 weeks, **could** you do the household shopping **on your own**?

yes, easily	with little difficulty	with moderate difficulty	with extreme difficulty	no, impossible
[ ]	[ ]	[ ]	[ ]	[ ]

Q12 During the past 4 weeks, **could** you walk down one flight of stairs?

yes, easily	with little difficulty	with moderate difficulty	with extreme difficulty	no, impossible
[ ]	[ ]	[ ]	[ ]	[ ]

Thank you for completing the questionnaire.

12 Month General Health

Instructions

Example

Q01 How strongly do you disagree with the following statements?

	all of the time	most of the time	some of the time	a little of the time	none of the time
a. did you feel full of life?	[ ]	[ ]	[✓]	[ ]	[ ]
b. have you been very nervous?	[ ]	[✓]	[ ]	[ ]	[ ]

Please begin answering the questions now.

Q01 In general, would you say your health is:

excellent	very good	good	fair	poor
[ ]	[ ]	[ ]	[ ]	[ ]

Q02 **Compared to one year ago**, how would you rate your health in general **now**?

much better now than one year ago	somewhat better now than one year ago	about the same as one year ago	somewhat worse now than one year ago	much worse than one year ago
[ ]	[ ]	[ ]	[ ]	[ ]

Q03 The following questions are about activities you might do during a typical day. Does your health **now** limit you in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a. **vigorous activities** such as running, lifting heavy objects, participating in strenuous sports	[ ]	[ ]	[ ]
b. **moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling or playing golf	[ ]	[ ]	[ ]
c. **lifting or carrying groceries**	[ ]	[ ]	[ ]
d. climbing **several** flights of stairs	[ ]	[ ]	[ ]
e. climbing **one** flight of stairs	[ ]	[ ]	[ ]
f. bending, kneeling or stooping	[ ]	[ ]	[ ]
g. walking **more than a mile**	[ ]	[ ]	[ ]
h. walking **several hundred yards**	[ ]	[ ]	[ ]
i. walking **one hundred yards**	[ ]	[ ]	[ ]
j. bathing or dressing yourself	[ ]	[ ]	[ ]

PTO

Q04 During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**?

	all of the time	most of the time	some of the time	a little of the time	none of the time
a. cut down on the **amount of time** you spent on work or other activities	[ ]	[ ]	[ ]	[ ]	[ ]
b. **accomplished less** than you would like	[ ]	[ ]	[ ]	[ ]	[ ]
c. were **limited** in the **kind** of work or other activities	[ ]	[ ]	[ ]	[ ]	[ ]
d. had **difficulty** performing the work or other activities *(eg. it took extra effort)*	[ ]	[ ]	[ ]	[ ]	[ ]

Q05 **During the past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

	all of the time	most of the time	some of the time	a little of the time	none of the time
a. cut down on the **amount of time** you spent on work or other activities	[ ]	[ ]	[ ]	[ ]	[ ]
b. **accomplished less** than you would like	[ ]	[ ]	[ ]	[ ]	[ ]
c. did work or other activities less **carefully** than usual	[ ]	[ ]	[ ]	[ ]	[ ]

Q06 During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours or groups?

not at all	slightly	moderately	quite a bit	extremely
[ ]	[ ]	[ ]	[ ]	[ ]

Q07 How much physical pain have you had **during the past 4 weeks**?

none	very mild	mild	moderate	severe	very severe
[ ]	[ ]	[ ]	[ ]	[ ]	[ ]

Q08 During the **past 4 weeks**, how much did **pain** interfere with your normal work? *(including both work outside the home and housework)*

not at all	slightly	moderately	quite a bit	extremely
[ ]	[ ]	[ ]	[ ]	[ ]

Q09 These questions are about how you feel and how things have been with you **during the past 4 weeks**. Please give the one answer that is closest to the way you have been feeling for each item. How much time during the **past 4 weeks**...

	all of the time	most of the time	some of the time	a little of the time	none of the time
a. did you feel full of life?	[ ]	[ ]	[ ]	[ ]	[ ]
b. have you been very nervous?	[ ]	[ ]	[ ]	[ ]	[ ]
c. have you felt so down in the dumps that nothing could cheer you up?	[ ]	[ ]	[ ]	[ ]	[ ]
d. have you felt calm and peaceful?	[ ]	[ ]	[ ]	[ ]	[ ]
e. did you have a lot of energy?	[ ]	[ ]	[ ]	[ ]	[ ]
f. have you felt depressed?	[ ]	[ ]	[ ]	[ ]	[ ]
g. did you feel worn out?	[ ]	[ ]	[ ]	[ ]	[ ]
h. have you been happy?	[ ]	[ ]	[ ]	[ ]	[ ]
i. did you feel tired?	[ ]	[ ]	[ ]	[ ]	[ ]

Q10 During the past 4 weeks, how much of the time has your **physical health or emotional problems** interfered with your social activities? *(like visiting with friends, relatives, etc.)*

all of the time	most of the time	some of the time	a little of the time	none of the time
[ ]	[ ]	[ ]	[ ]	[ ]

Q11 How TRUE or FALSE is **each** of the following statements for you?

	definitely true	mostly true	don't know	mostly false	definitely false
a. I seem to get sick a little easier than other people	[ ]	[ ]	[ ]	[ ]	[ ]
b. I am as healthy as anybody I know	[ ]	[ ]	[ ]	[ ]	[ ]
c. I expect my health to get worse	[ ]	[ ]	[ ]	[ ]	[ ]
d. my health is excellent	[ ]	[ ]	[ ]	[ ]	[ ]

KNEE OUTCOME PREDICTION STUDY

study number

form 17

12 Month Satisfaction Score

Q01 Knowing what you know now, would you still choose to have the operation on your knee?

[ ] yes [ ] no

Q02 How likely are you to recommend a total knee replacement to friends and family if they needed similar care or treatment?

extremely likely	likely	neither likely nor unlikely	unlikely	extremely unlikely	don't know
[ ]	[ ]	[ ]	[ ]	[ ]	[ ]

Q03 How satisfied are you with the results of your surgery?

very satisfied	somewhat satisfied	somewhat dissatisfied	very dissatisfied
[ ]	[ ]	[ ]	[ ]

Q04 How satisfied are you with the results of your surgery for improving your pain?

very satisfied	somewhat satisfied	somewhat dissatisfied	very dissatisfied
[ ]	[ ]	[ ]	[ ]

Q05 How satisfied are you with the results of your surgery for improving your ability to look after yourself?

very satisfied	somewhat satisfied	somewhat dissatisfied	very dissatisfied
[ ]	[ ]	[ ]	[ ]

Q06 How satisfied are you with the results of your surgery for improving your ability to do recreational activities?

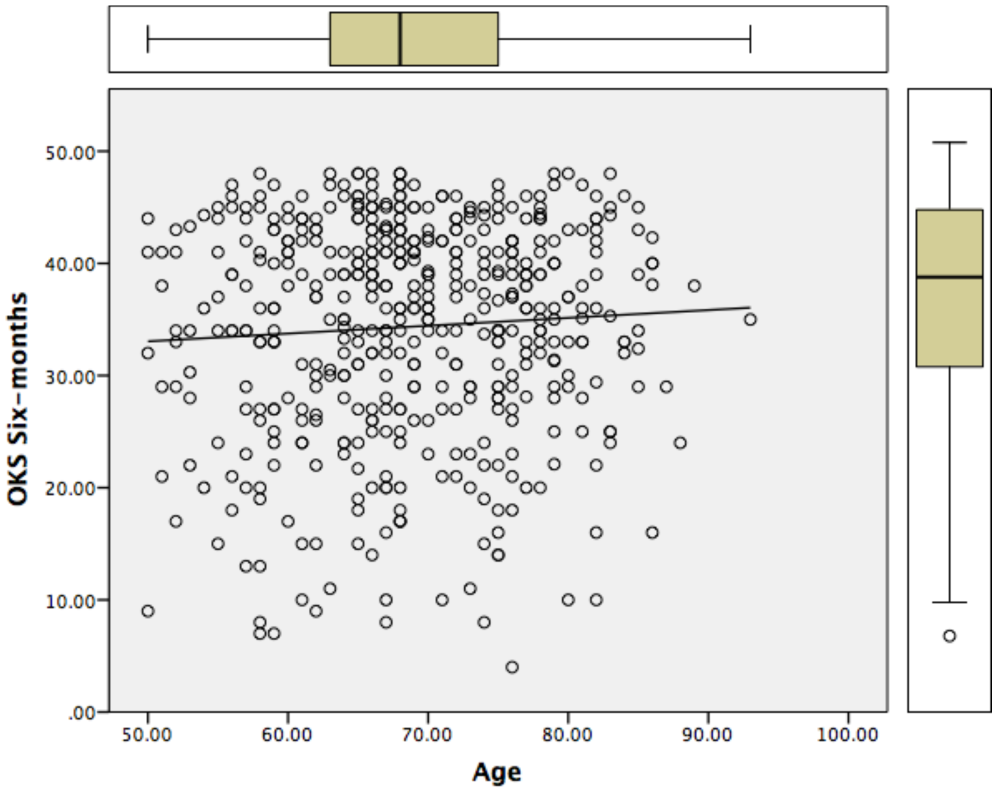
very satisfied	somewhat satisfied	somewhat dissatisfied	very dissatisfied
[ ]	[ ]	[ ]	[ ]

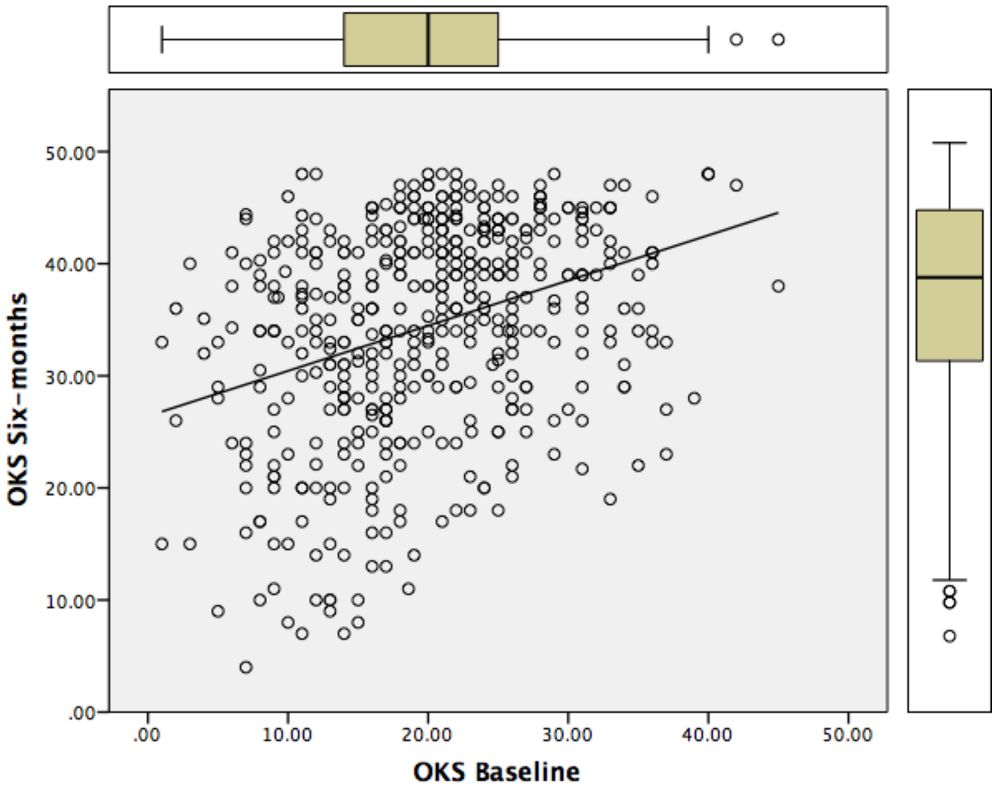
Thank you for completing this questionnaire.

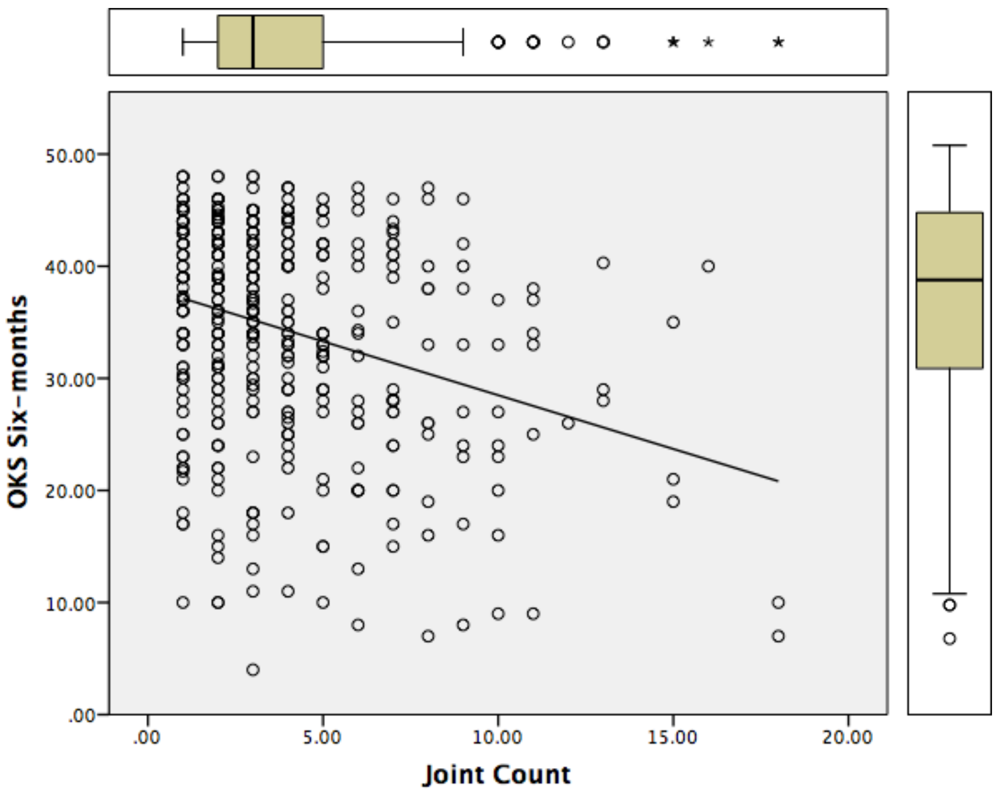
9.6 Appendix VI: Appendix for the results

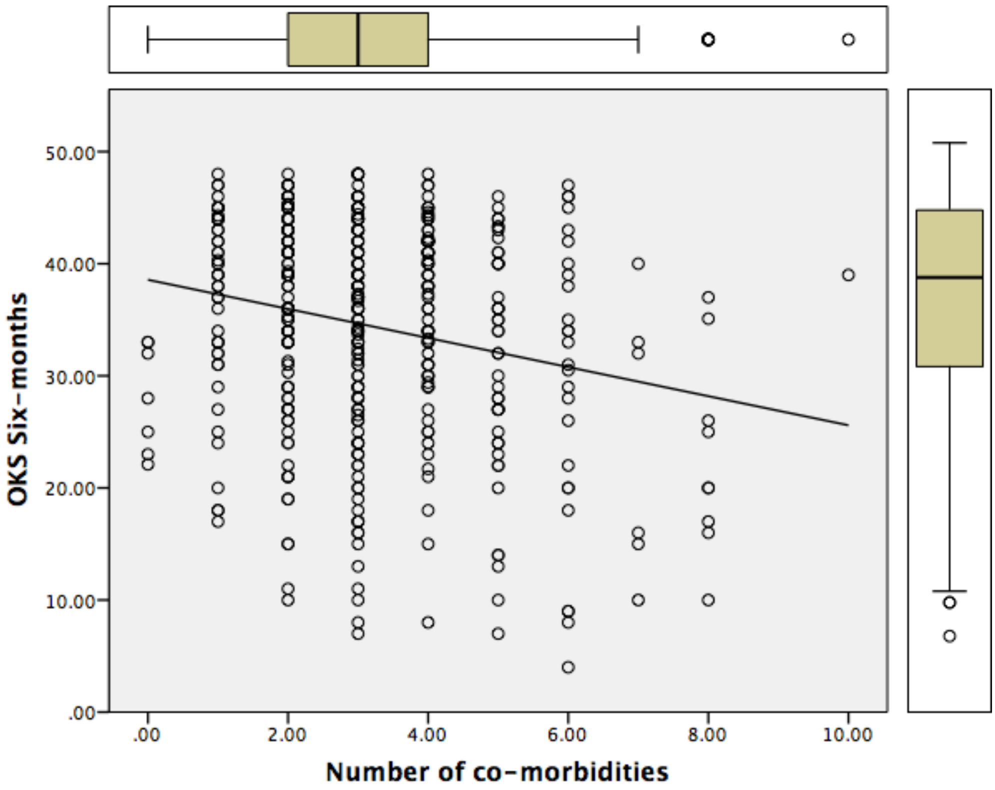
Six month data analysis

Linearity of explanatory variables to response variables was visually assessed using scatterplots of each explanatory scale variable against OKS at six months.

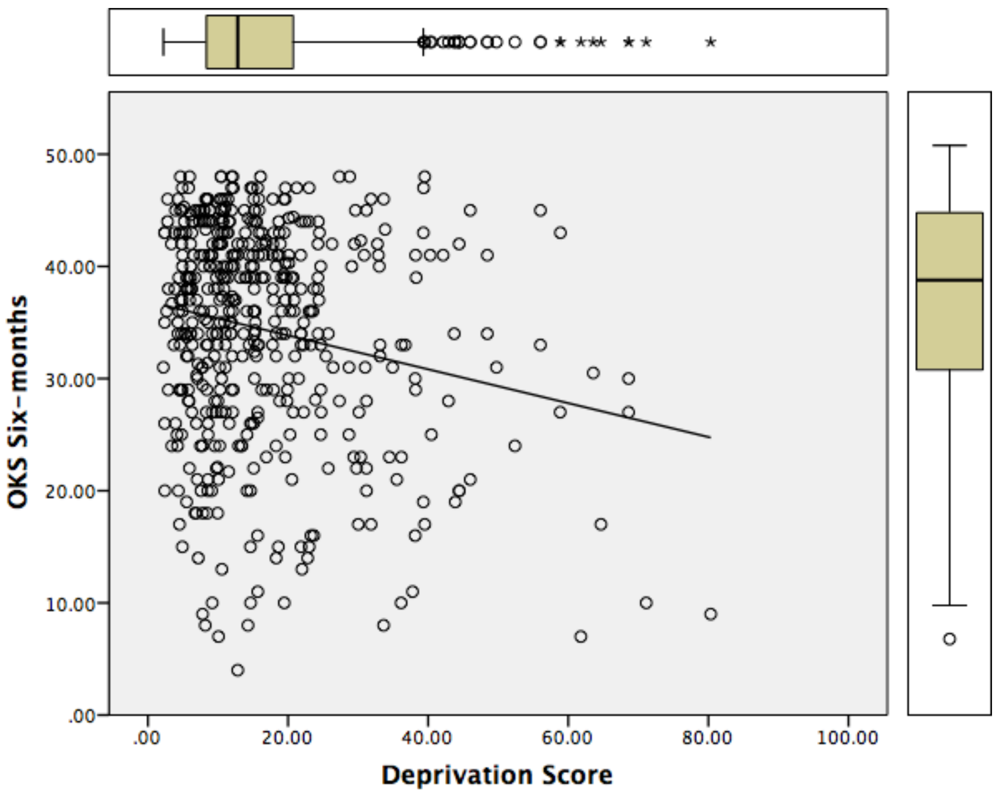



50.00
40.00
30.00
20.00
10.00
.00
OKS Six-months
.00
10.00
20.00
30.00
40.00
50.00
OKS Baseline

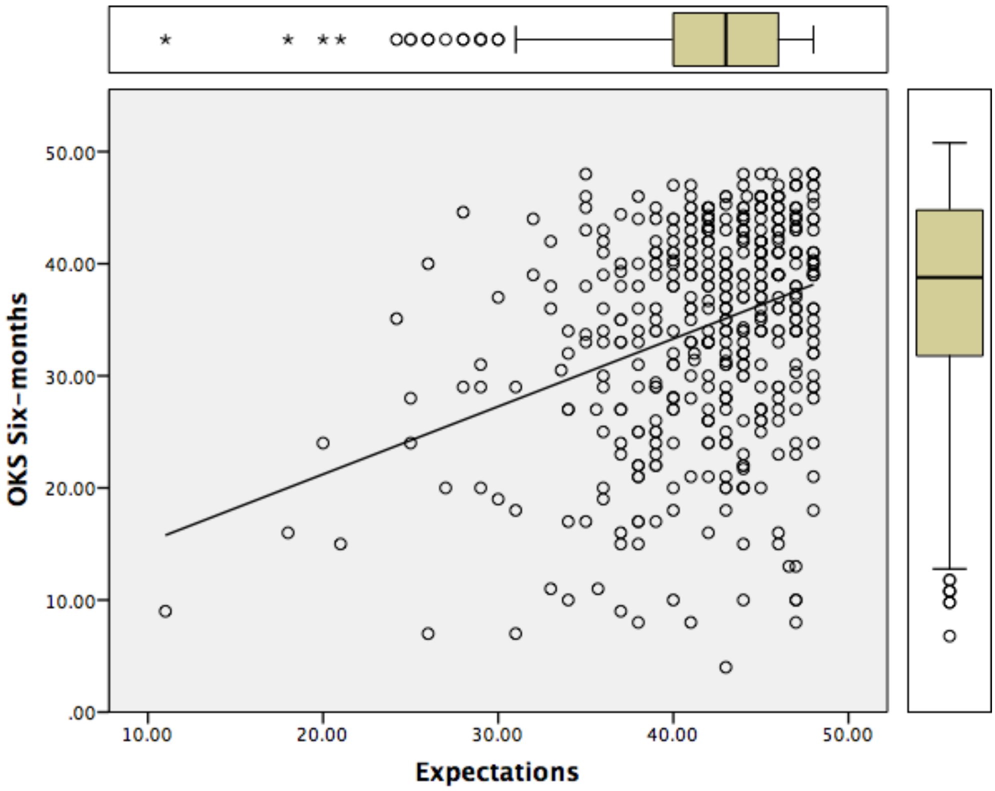

50.00
40.00
30.00
20.00
10.00
.00
OKS Six-months
.00
5.00
10.00
15.00
20.00
Joint Count

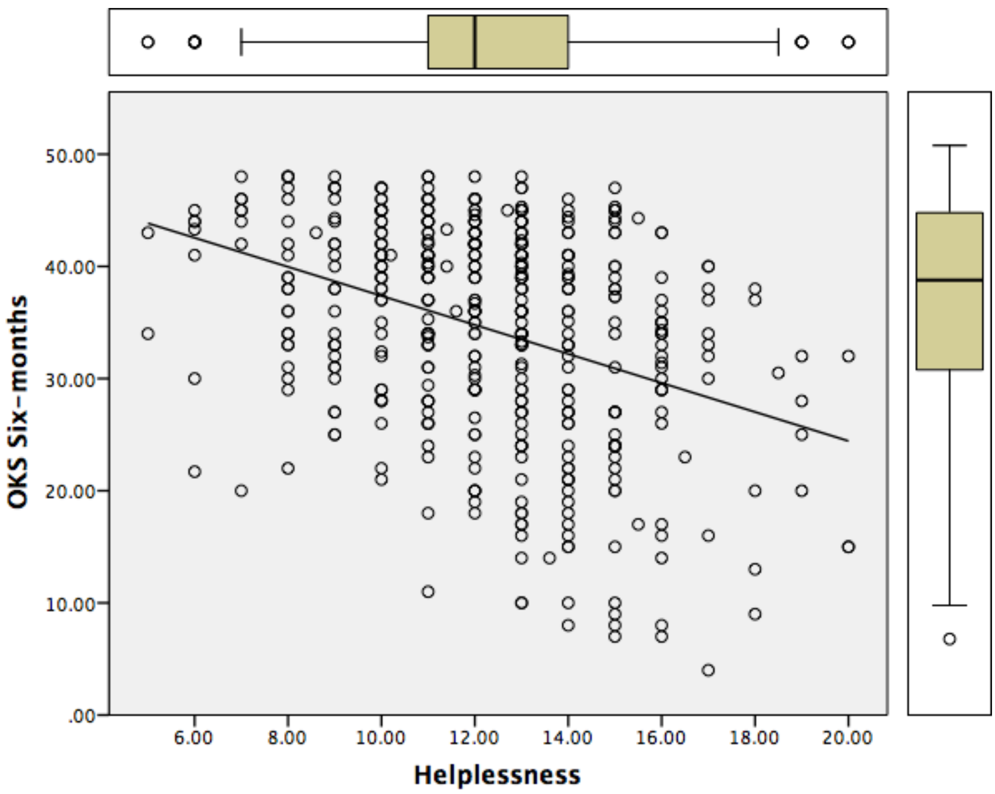


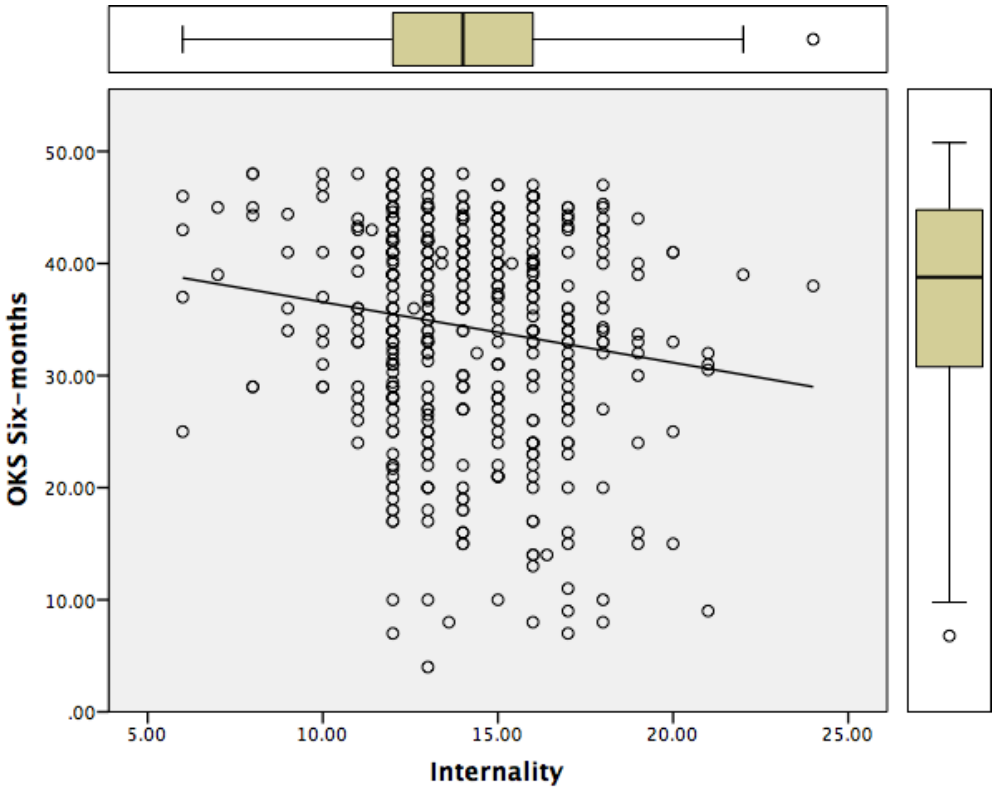
OKS Six-months
50.00
40.00
30.00
20.00
10.00
.00
.00
2.00
4.00
6.00
8.00
10.00
Number of co-morbidities

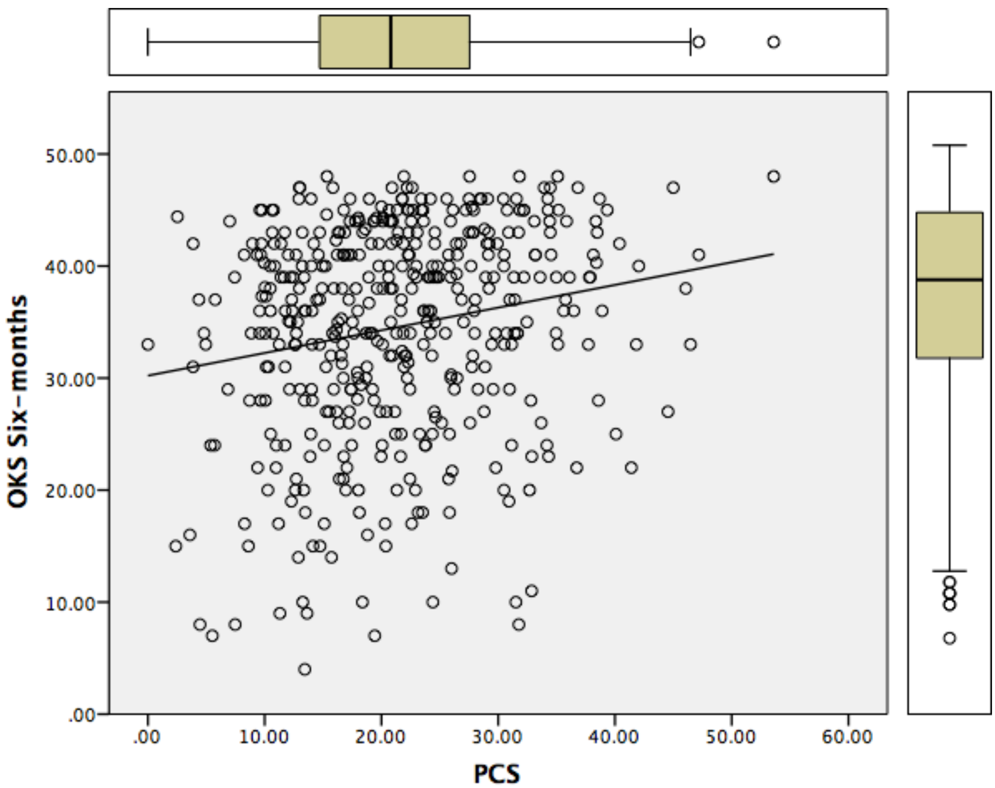


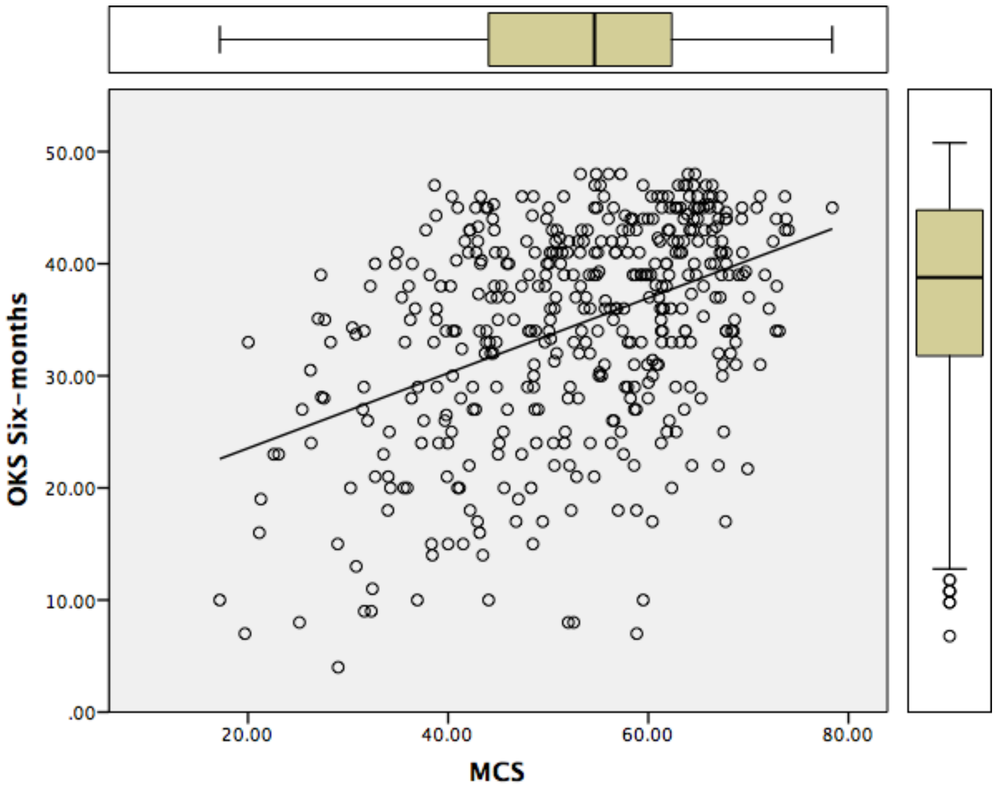
OKS Six-months
50.00
40.00
30.00
20.00
10.00
.00
.00
20.00
40.00
60.00
80.00
100.00
Deprivation Score


OKS Six-months
Expectations
50.00
40.00
30.00
20.00
10.00
.00
10.00
20.00
30.00
40.00
50.00


OKS Six-months
Helplessness
50.00
40.00
30.00
20.00
10.00
.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00
20.00


50.00
40.00
30.00
20.00
10.00
.00
OKS Six-months
5.00
10.00
15.00
20.00
25.00
Internality


50.00
40.00
30.00
20.00
10.00
.00
OKS Six-months
.00
10.00
20.00
30.00
40.00
50.00
60.00
PCS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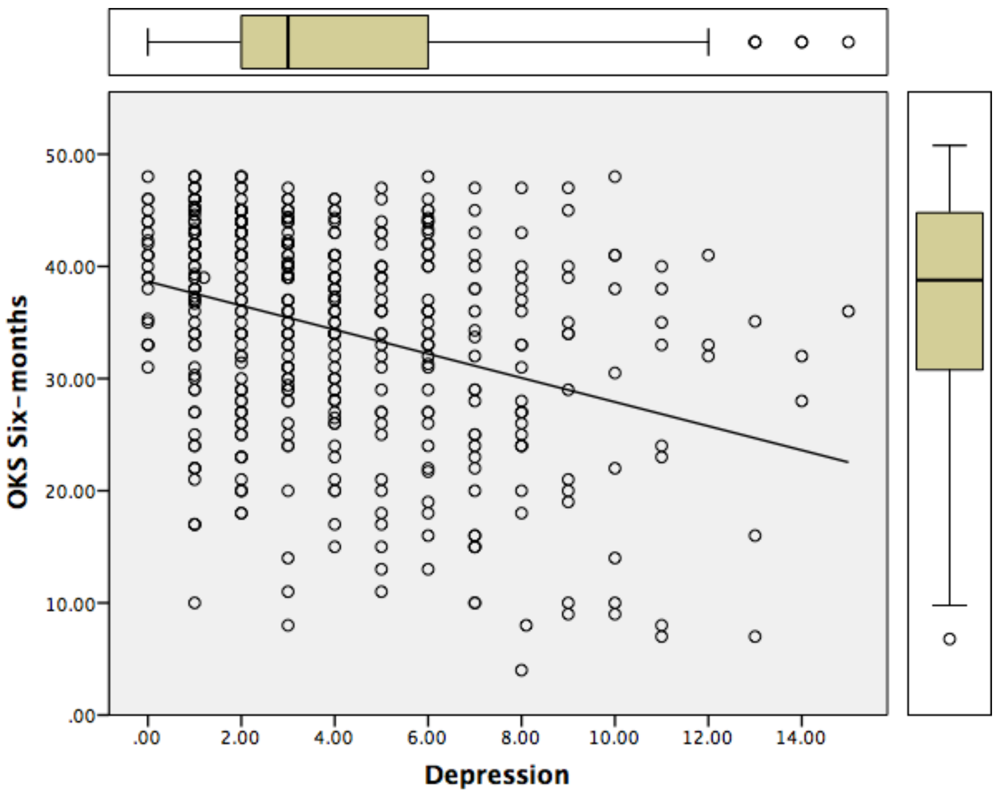
OKS Six-months
20.00
40.00
60.00
80.00
MCS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40.00
30.00
20.00
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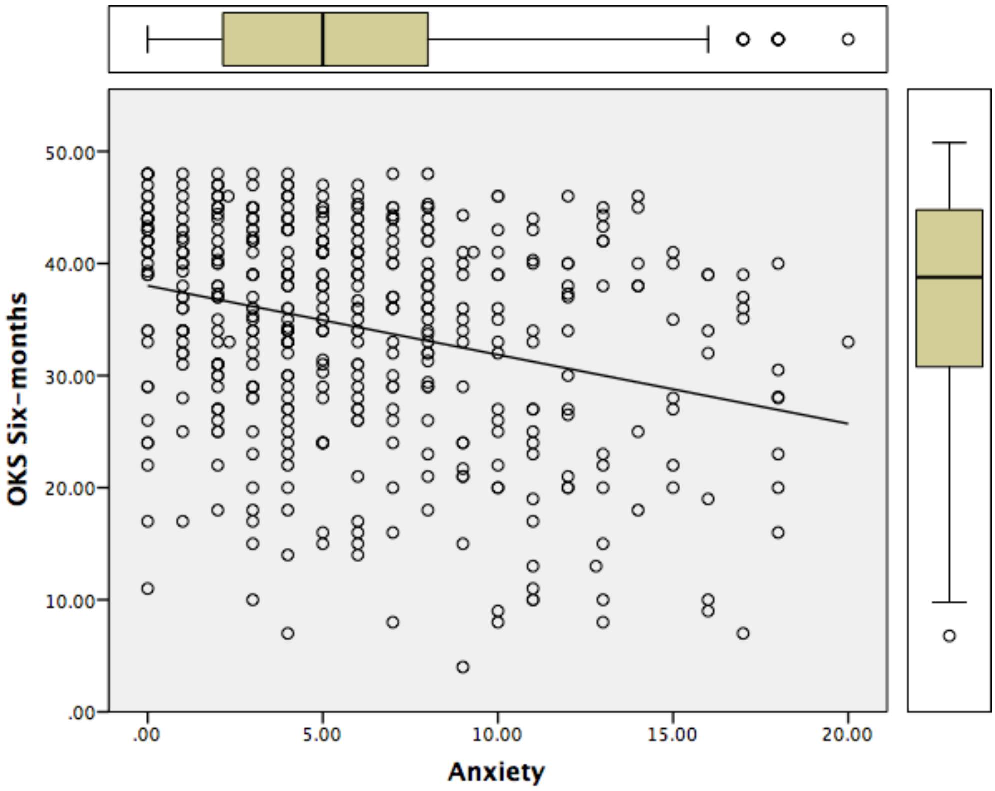
.00
OKS Six-months
.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00
Depression


50.00
40.00
30.00
20.00
10.00
.00
OKS Six-months
.00
5.00
10.00
15.00
20.00
Anxiety

Multicollinearity

Correlation co-efficients between each variable are displayed below (Table continued over next six pages)

		OKS Six months	Age	Gender	OKS Baseline	BMI	Severe Arthritis	Joint Count	Lower back pain	Number of co-morbidities	Live Alone
Pearson Correlation	OKS Six months	1	0.062	-0.07	0.336	-0.142	0.153	-0.294	-0.178	-0.216	0.044
	Age	0.062	1	-0.064	0.032	-0.32	0.151	-0.162	-0.087	0.005	0.236
	Female Gender	-0.07	-0.064	1	-0.197	0.137	-0.111	0.222	0.127	0.143	0.189
	OKS Baseline	0.336	0.032	-0.197	1	-0.197	0.051	-0.311	-0.206	-0.274	-0.04
	BMI	-0.142	-0.32	0.137	-0.197	1	-0.075	0.206	0.119	0.223	-0.059
	Severe Arthritis	0.153	0.151	-0.111	0.051	-0.075	1	-0.115	-0.097	-0.088	0.068
	Joint Count	-0.294	-0.162	0.222	-0.311	0.206	-0.115	1	0.441	0.36	0.032
	Lower back pain	-0.178	-0.087	0.127	-0.206	0.119	-0.097	0.441	1	0.324	0.035
	Co-morbidities	-0.216	0.005	0.143	-0.274	0.223	-0.088	0.36	0.324	1	0.102
	Live Alone	0.044	0.236	0.189	-0.04	-0.059	0.068	0.032	0.035	0.102	1
	Deprivation Score	-0.193	-0.098	-0.015	-0.191	0.109	-0.152	0.199	0.161	0.17	-0.002
	Previous Arthroscopy	-0.039	-0.179	-0.041	0.013	0.055	-0.077	0.004	0.062	-0.015	-0.096
	Expectations	0.324	-0.06	-0.125	0.325	-0.123	0.024	-0.318	-0.188	-0.358	-0.051
	Helplessness	-0.36	0.03	0.165	-0.553	0.078	-0.075	0.261	0.112	0.297	0.016
	Internality	-0.148	-0.064	0.096	-0.3	0.051	0.003	0.114	0.001	0.135	0.037
	PCS	0.191	-0.094	-0.139	0.659	-0.14	-0.016	-0.21	-0.196	-0.233	0.014
	MCS	0.428	0.07	-0.263	0.435	-0.164	0.157	-0.335	-0.148	-0.36	-0.087
	Depression	-0.327	-0.027	0.103	-0.355	0.138	-0.056	0.251	0.138	0.322	0.044
	Anxiety	-0.283	-0.09	0.281	-0.347	0.113	-0.116	0.3	0.169	0.339	0.112

Multicollinearity table (cont.)

		OKS Six months	Age	Gender	OKS Baseline	BMI	Severe Arthritis	Joint Count	Lower back pain	Number of co-morbidities	Live Alone
Sig. (1-tailed)	OKS Six months	.	0.086	0.061	0	0.001	0	0	0	0	0.177
	Age	0.086	.	0.074	0.24	0	0	0	0.032	0.458	0
	Gender	0.061	0.074	.	0	0.002	0.006	0	0.003	0.001	0
	OKS Baseline	0	0.24	0	.	0	0.131	0	0	0	0.192
	BMI	0.001	0	0.002	0	.	0.058	0	0.008	0	0.108
	Severe Arthritis	0	0	0.006	0.131	0.058	.	0.008	0.022	0.028	0.073
	Joint Count	0	0	0	0	0	0.008	.	0	0	0.254
	Lower back pain	0	0.032	0.003	0	0.008	0.022	0	.	0	0.238
	Number of co-morbidities	0	0.458	0.001	0	0	0.028	0	0	.	0.014
	Live Alone	0.177	0	0	0.192	0.108	0.073	0.254	0.238	0.014	.
	Deprivation Score	0	0.013	0.368	0	0.01	0	0	0	0	0.481
	Previous Arthroscopy	0.214	0	0.193	0.393	0.131	0.055	0.465	0.109	0.377	0.023
	Expectations	0	0.094	0.003	0	0.005	0.301	0	0	0	0.139
	Helplessness	0	0.254	0	0	0.054	0.052	0	0.01	0	0.369
	Internality	0.001	0.08	0.017	0	0.144	0.475	0.009	0.496	0.002	0.213
	PCS	0	0.021	0.001	0	0.002	0.369	0	0	0	0.386
	MCS	0	0.065	0	0	0	0	0	0.001	0	0.035
	Depression	0	0.274	0.011	0	0.002	0.111	0	0.002	0	0.178
	Anxiety	0	0.024	0	0	0.01	0.006	0	0	0	0.008

Multicollinearity table (cont.)

		OKS Six months	Age	Gender	OKS Baseline	BMI	Severe Arthritis	Joint Count	Lower back pain	Number of co-morbidities	Live Alone
N	OKS Six months	489	489	489	475	432	478	429	429	463	454
	Age	489	517	517	502	457	501	451	451	487	481
	Gender	489	517	517	502	457	501	451	451	487	481
	OKS Baseline	475	502	502	502	446	486	437	437	475	470
	BMI	432	457	457	446	457	441	405	405	435	440
	Severe Arthritis	478	501	501	486	441	501	438	438	473	465
	Joint Count	429	451	451	437	405	438	451	451	437	424
	Lower back pain	429	451	451	437	405	438	451	451	437	424
	Number of co-morbidities	463	487	487	475	435	473	437	437	487	456
	Live Alone	454	481	481	470	440	465	424	424	456	481
	Deprivation Score	489	517	517	502	457	501	451	451	487	481
	Previous Arthroscopy	425	452	452	441	414	438	402	402	431	439
	Expectations	461	488	488	475	432	473	431	431	464	456
	Helplessness	459	485	485	475	431	469	426	426	464	452
	Internality	459	485	485	475	431	469	427	427	464	452
	PCS	441	466	466	461	413	451	414	414	442	433
	MCS	441	466	466	461	413	451	414	414	442	433
	Depression	463	488	488	475	432	474	432	432	464	454
	Anxiety	464	490	490	476	434	475	433	433	465	456

Multicollinearity table (cont.)

		Deprivation Score	Previous Arthroscopy	Expectations	Helplessness	Internality	PCS	MCS	Depression	Anxiety
Pearson Correlation	OKS Six months	-0.193	-0.039	0.324	-0.36	-0.148	0.191	0.428	-0.327	-0.283
	Age	-0.098	-0.179	-0.06	0.03	-0.064	-0.094	0.07	-0.027	-0.09
	Gender	-0.015	-0.041	-0.125	0.165	0.096	-0.139	-0.263	0.103	0.281
	OKS Baseline	-0.191	0.013	0.325	-0.553	-0.3	0.659	0.435	-0.355	-0.347
	BMI	0.109	0.055	-0.123	0.078	0.051	-0.14	-0.164	0.138	0.113
	Severe Arthritis	-0.152	-0.077	0.024	-0.075	0.003	-0.016	0.157	-0.056	-0.116
	Joint Count	0.199	0.004	-0.318	0.261	0.114	-0.21	-0.335	0.251	0.3
	Lower back pain	0.161	0.062	-0.188	0.112	0.001	-0.196	-0.148	0.138	0.169
	Number of co-morbidities	0.17	-0.015	-0.358	0.297	0.135	-0.233	-0.36	0.322	0.339
	Live Alone	-0.002	-0.096	-0.051	0.016	0.037	0.014	-0.087	0.044	0.112
	Deprivation Score	1	0.014	-0.137	0.13	0.124	-0.023	-0.239	0.203	0.204
	Previous Arthroscopy	0.014	1	0.062	-0.019	0.089	0.019	-0.029	0.024	-0.035
	Expectations	-0.137	0.062	1	-0.3	-0.072	0.292	0.267	-0.244	-0.255
	Helplessness	0.13	-0.019	-0.3	1	0.369	-0.405	-0.495	0.424	0.412
	Internality	0.124	0.089	-0.072	0.369	1	-0.191	-0.277	0.3	0.174
	PCS	-0.023	0.019	0.292	-0.405	-0.191	1	0.018	-0.195	-0.092
	MCS	-0.239	-0.029	0.267	-0.495	-0.277	0.018	1	-0.59	-0.699
	Depression	0.203	0.024	-0.244	0.424	0.3	-0.195	-0.59	1	0.548
	Anxiety	0.204	-0.035	-0.255	0.412	0.174	-0.092	-0.699	0.548	1

Multicollinearity table (cont.)

		Deprivation Score	Previous Arthroscopy	Expectations	Helplessness	Internality	PCS	MCS	Depression	Anxiety
Sig. (1-tailed)	OKS Six months	0	0.214	0	0	0.001	0	0	0	0
	Age	0.013	0	0.094	0.254	0.08	0.021	0.065	0.274	0.024
	Gender	0.368	0.193	0.003	0	0.017	0.001	0	0.011	0
	OKS Baseline	0	0.393	0	0	0	0	0	0	0
	BMI	0.01	0.131	0.005	0.054	0.144	0.002	0	0.002	0.01
	Severe Arthritis	0	0.055	0.301	0.052	0.475	0.369	0	0.111	0.006
	Joint Count	0	0.465	0	0	0.009	0	0	0	0
	Lower back pain	0	0.109	0	0.01	0.496	0	0.001	0.002	0
	Number of co-morbidities	0	0.377	0	0	0.002	0	0	0	0
	Live Alone	0.481	0.023	0.139	0.369	0.213	0.386	0.035	0.178	0.008
	Deprivation Score	.	0.381	0.001	0.002	0.003	0.312	0	0	0
	Previous Arthroscopy	0.381	.	0.099	0.347	0.033	0.353	0.277	0.308	0.232
	Expectations	0.001	0.099	.	0	0.062	0	0	0	0
	Helplessness	0.002	0.347	0	.	0	0	0	0	0
	Internality	0.003	0.033	0.062	0	.	0	0	0	0
	PCS	0.312	0.353	0	0	0	.	0.348	0	0.026
	MCS	0	0.277	0	0	0	0.348	.	0	0
	Depression	0	0.308	0	0	0	0	0	.	0
	Anxiety	0	0.232	0	0	0	0.026	0	0	.

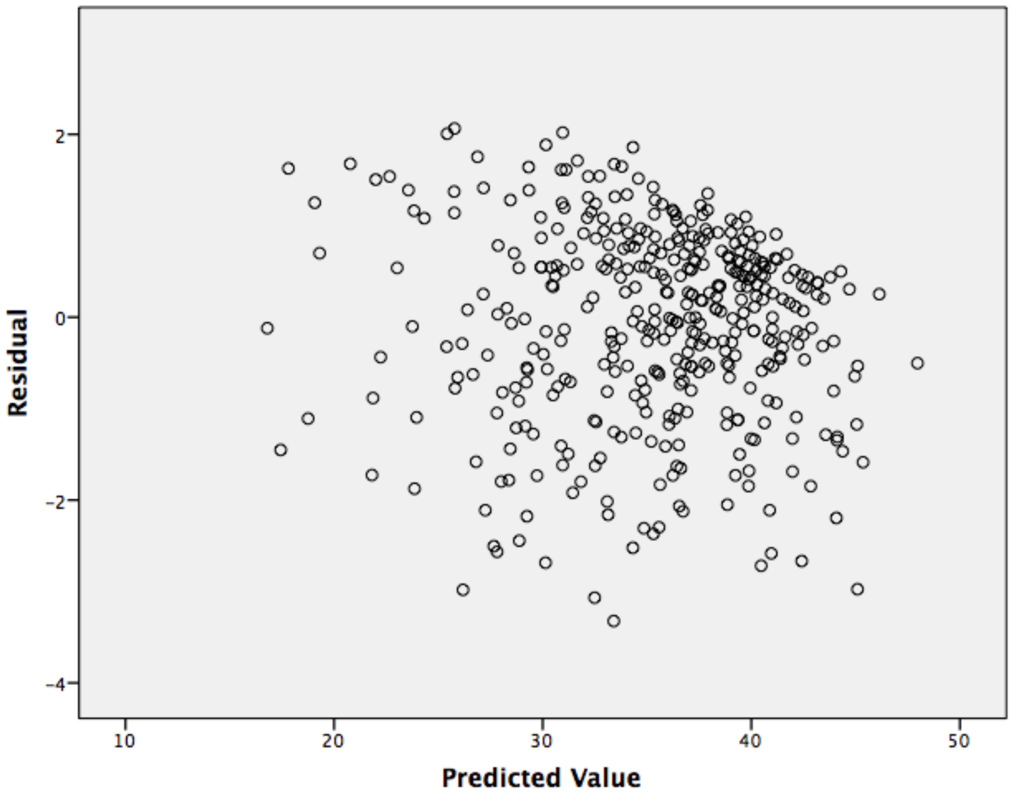
Multicollinearity table (cont.)

		Deprivation Score	Previous Arthroscopy	Expectations	Helplessness	Internality	PCS	MCS	Depression	Anxiety
N	OKS Six months	489	425	461	459	459	441	441	463	464
	Age	517	452	488	485	485	466	466	488	490
	Gender	517	452	488	485	485	466	466	488	490
	OKS Baseline	502	441	475	475	475	461	461	475	476
	BMI	457	414	432	431	431	413	413	432	434
	Severe Arthritis	501	438	473	469	469	451	451	474	475
	Joint Count	451	402	431	426	427	414	414	432	433
	Lower back pain	451	402	431	426	427	414	414	432	433
	Number of co-morbidities	487	431	464	464	464	442	442	464	465
	Live Alone	481	439	456	452	452	433	433	454	456
	Deprivation Score	517	452	488	485	485	466	466	488	490
	Previous Arthroscopy	452	452	427	429	431	410	410	429	431
	Expectations	488	427	488	463	463	444	444	474	475
	Helplessness	485	429	463	485	481	443	443	465	466
	Internality	485	431	463	481	485	444	444	465	466
	PCS	466	410	444	443	444	466	466	444	444
	MCS	466	410	444	443	444	466	466	444	444
	Depression	488	429	474	465	465	444	444	488	488
	Anxiety	490	431	475	466	466	444	444	488	490

Homoscedasticity of residuals

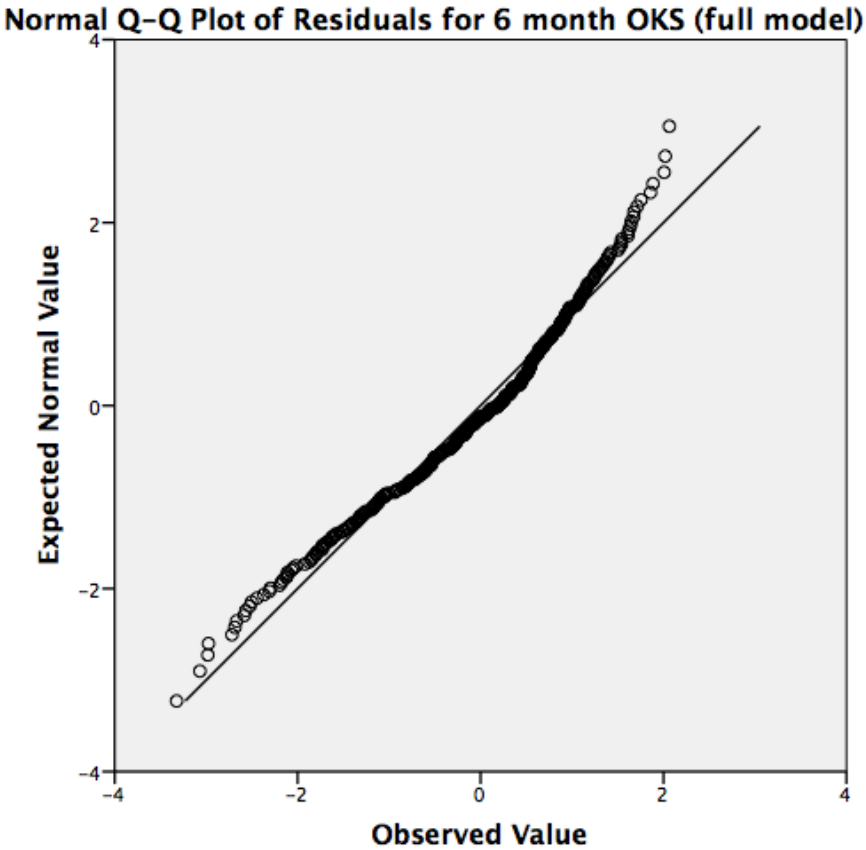
This was tested using a residual versus prediction scatterplot. An even spread of residual values across the range of predicted values suggests heteroscedasticity and linearity.

Residual against Predicted values



Normality of residuals

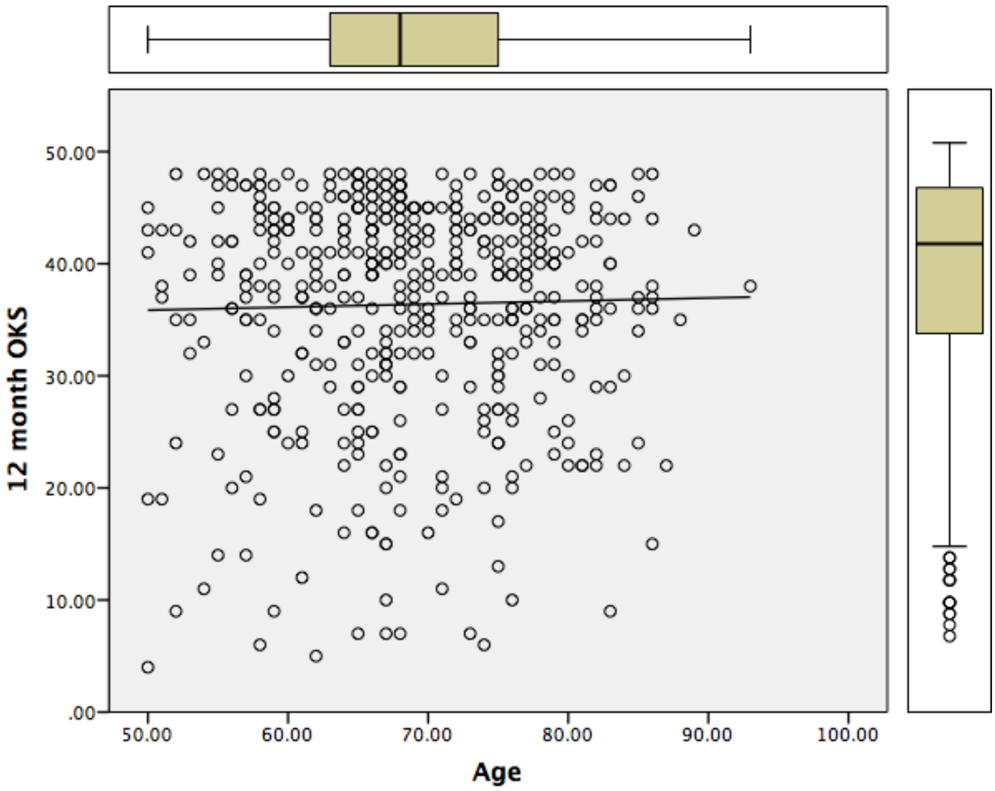
Normality of residuals was assessed informally using QQ plots:

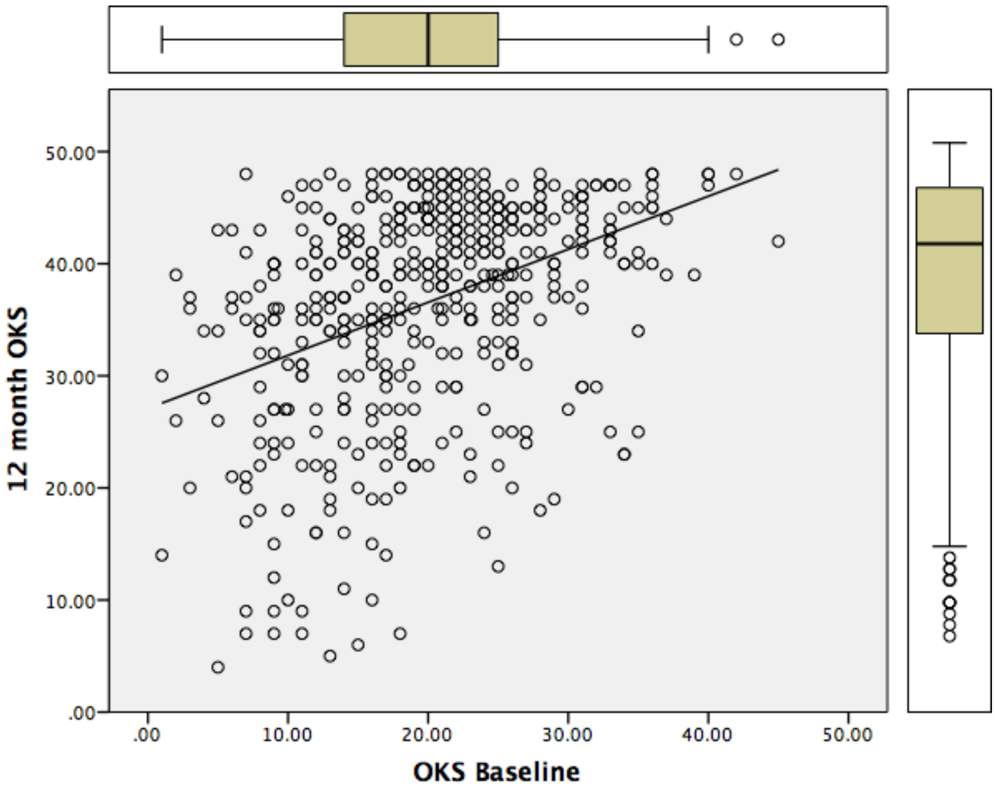

Normal Q-Q Plot of Residuals for 6 month OKS (full model)
Expected Normal Value
Observed Value
4
2
0
-2
-4
-4
-2
0
2
4

12 month data analysis

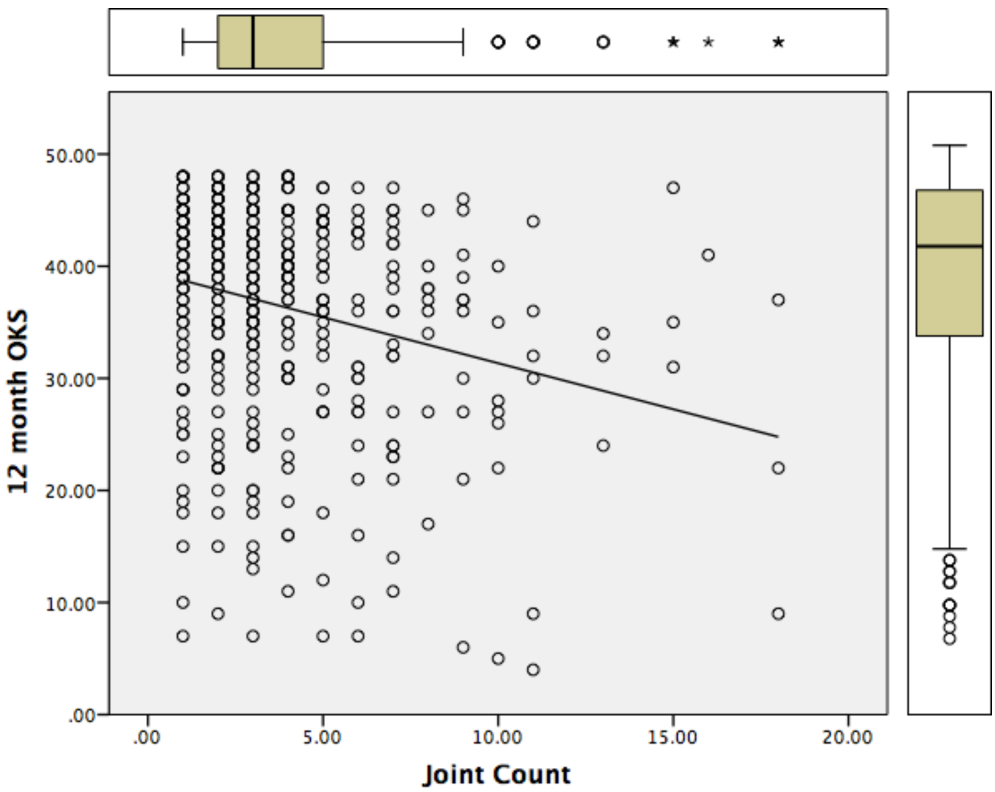
Scatterplots of each explanatory variable against each scale response variable is plotted below:

12 month OKS

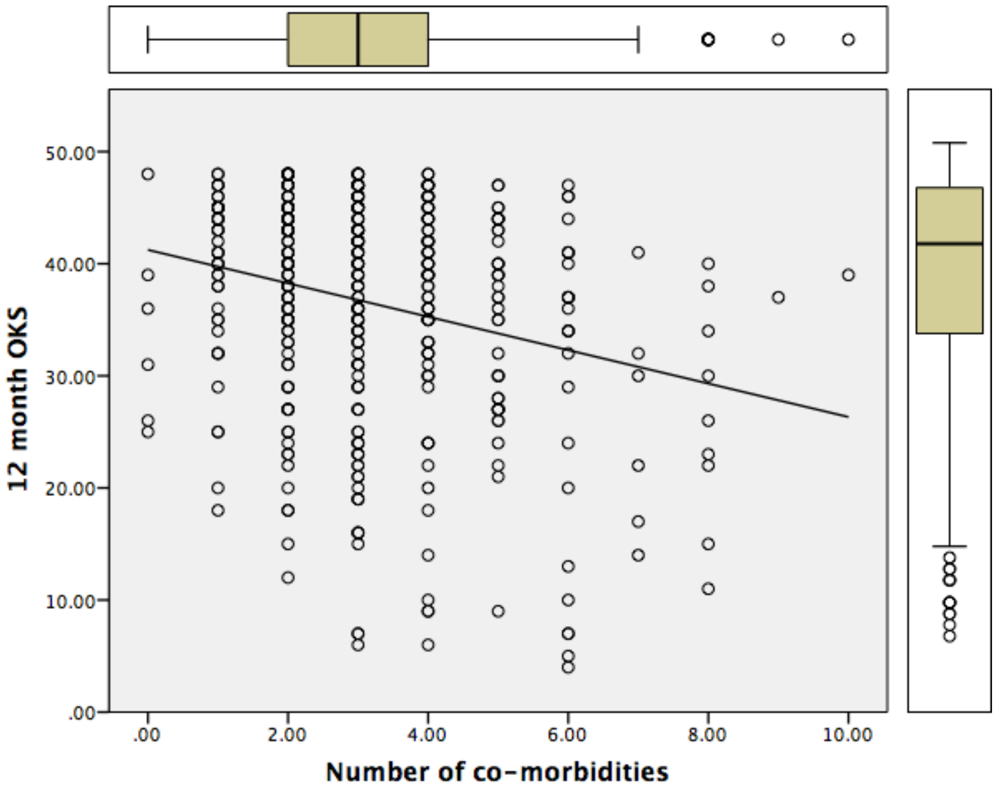


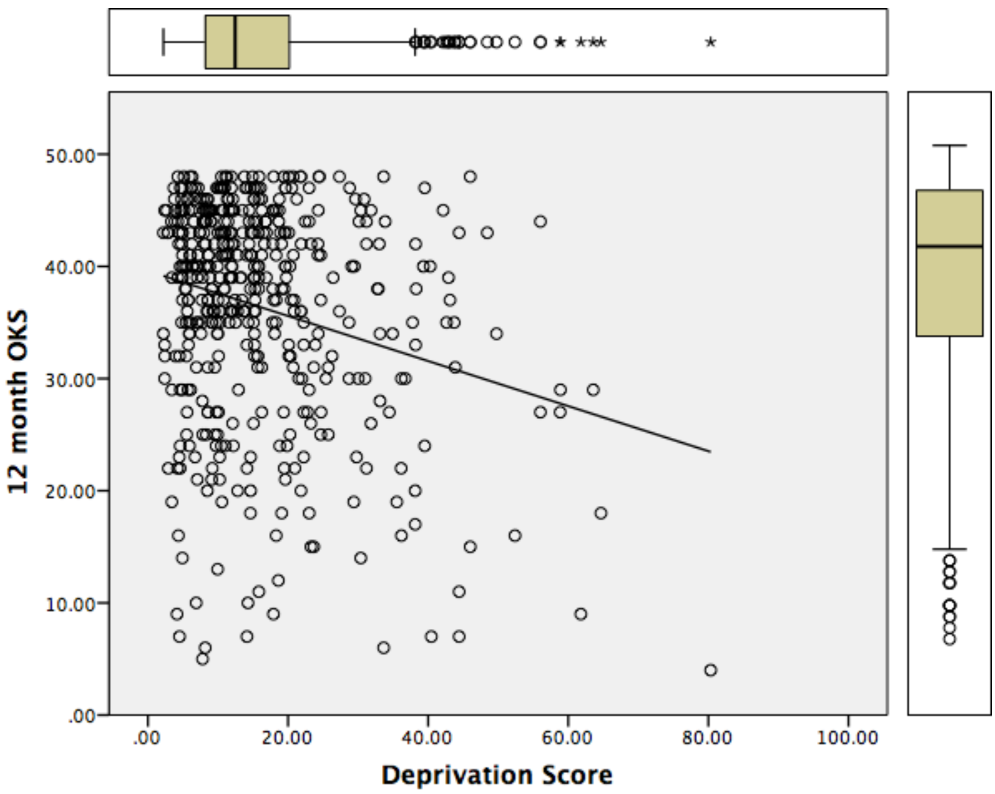


50.00
40.00
30.00
20.00
10.00
.00
12 month OKS
.00
10.00
20.00
30.00
40.00
50.00
OKS Baseline



50.00
40.00
30.00
20.00
10.00
.00
12 month OKS
.00
5.00
10.00
15.00
20.00
Joint Count


12 month OKS
Number of co-morbidities
50.00
40.00
30.00
20.00
10.00
.00
2.00
4.00
6.00
8.00
10.00


12 month OKS
Deprivation Score
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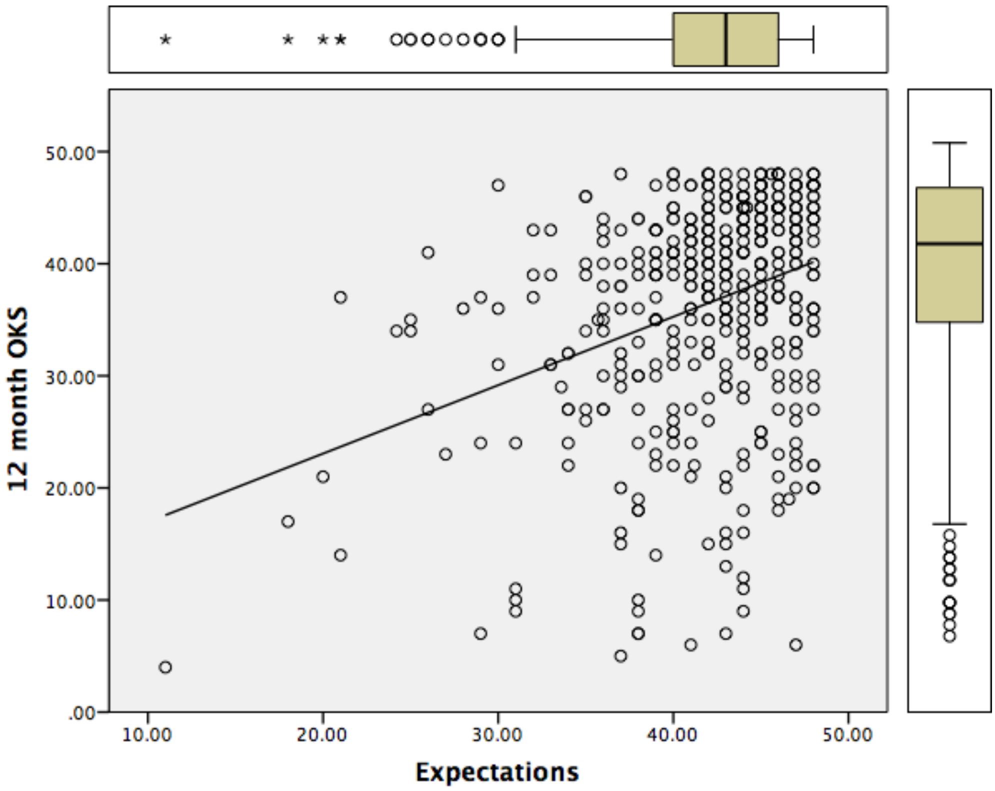
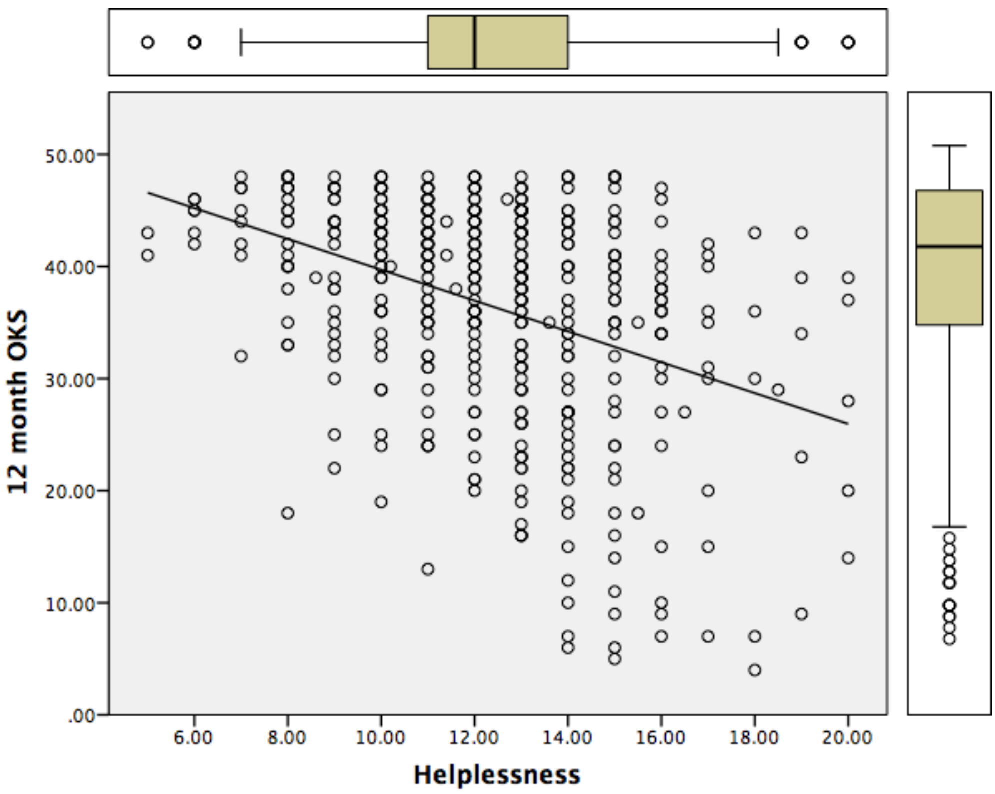
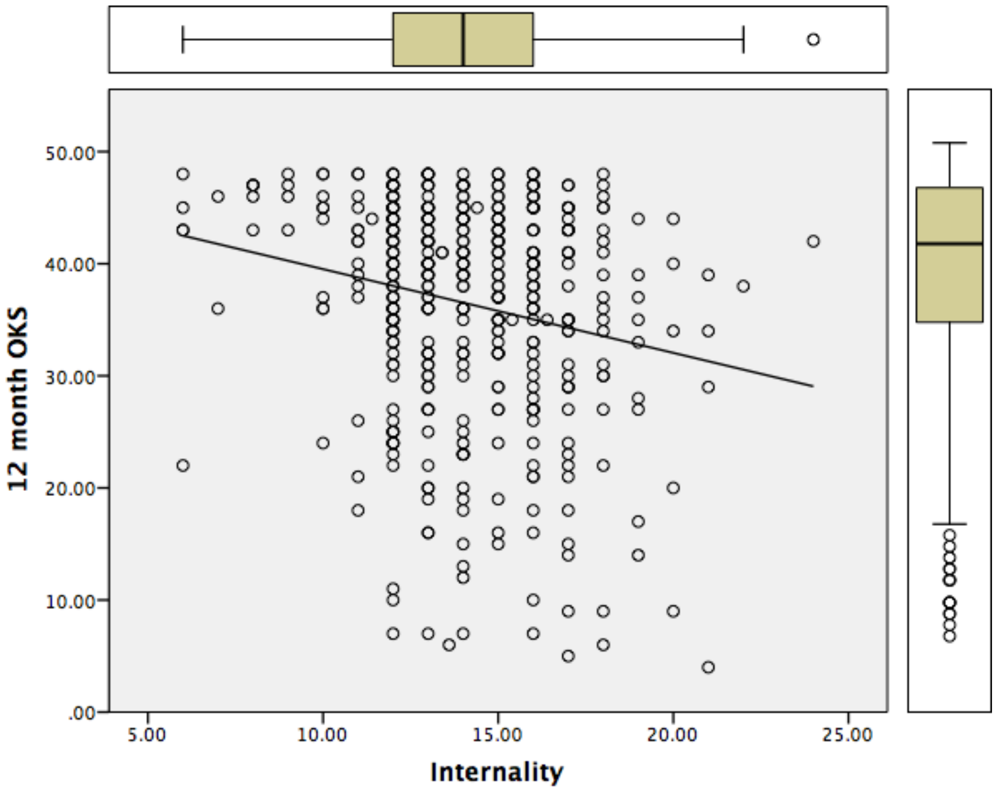
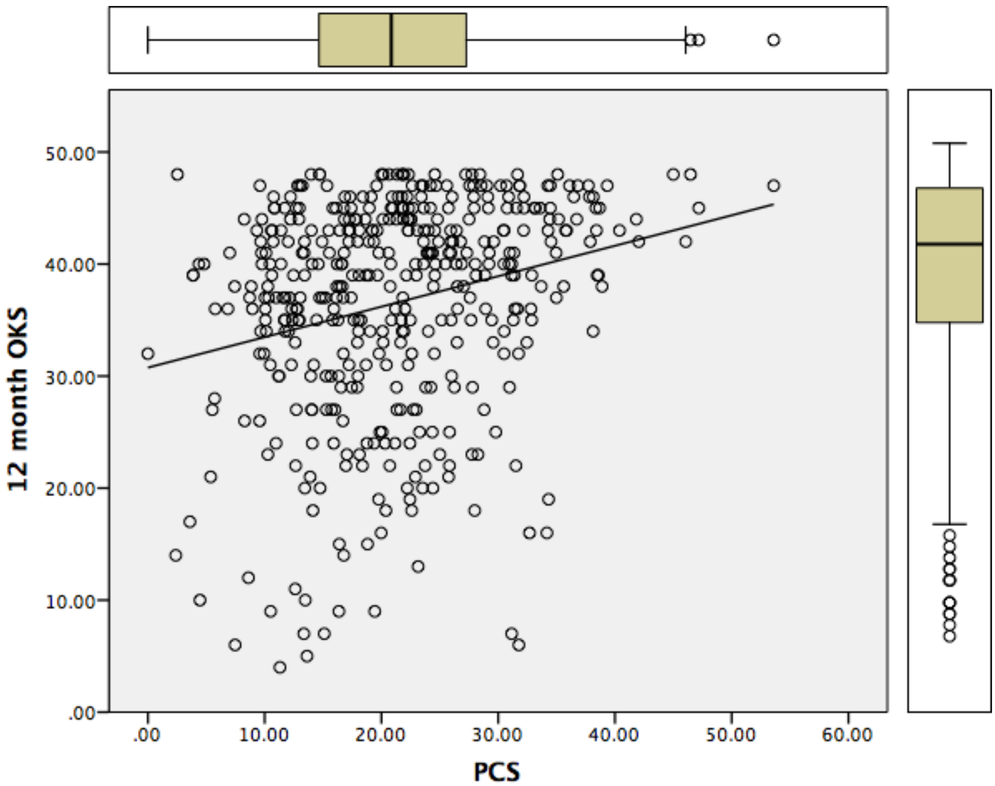
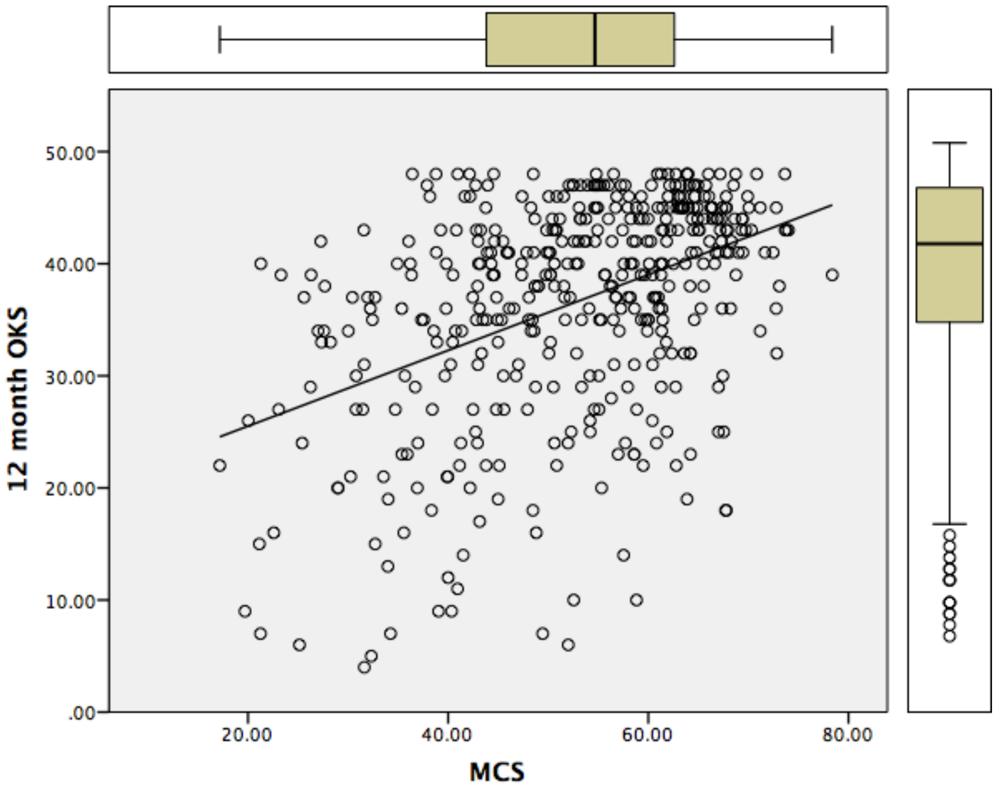
40.00
30.00
20.00
10.00
.00
20.00
40.00
60.00
80.00
100.00

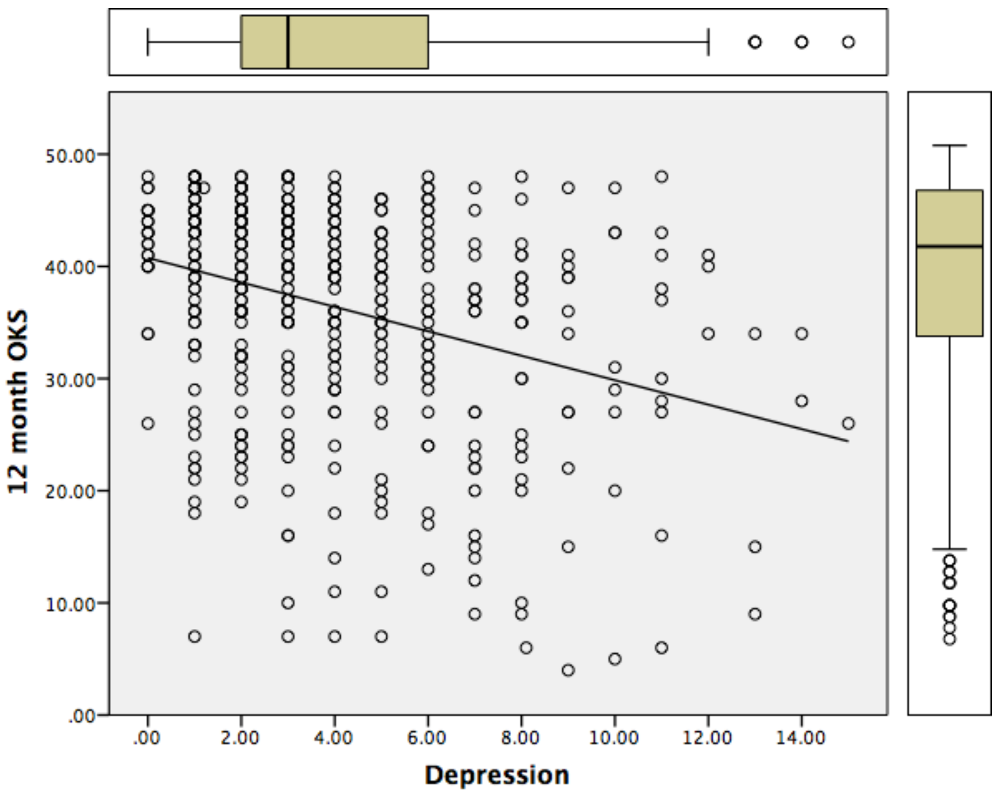

12 month OKS
Expectations

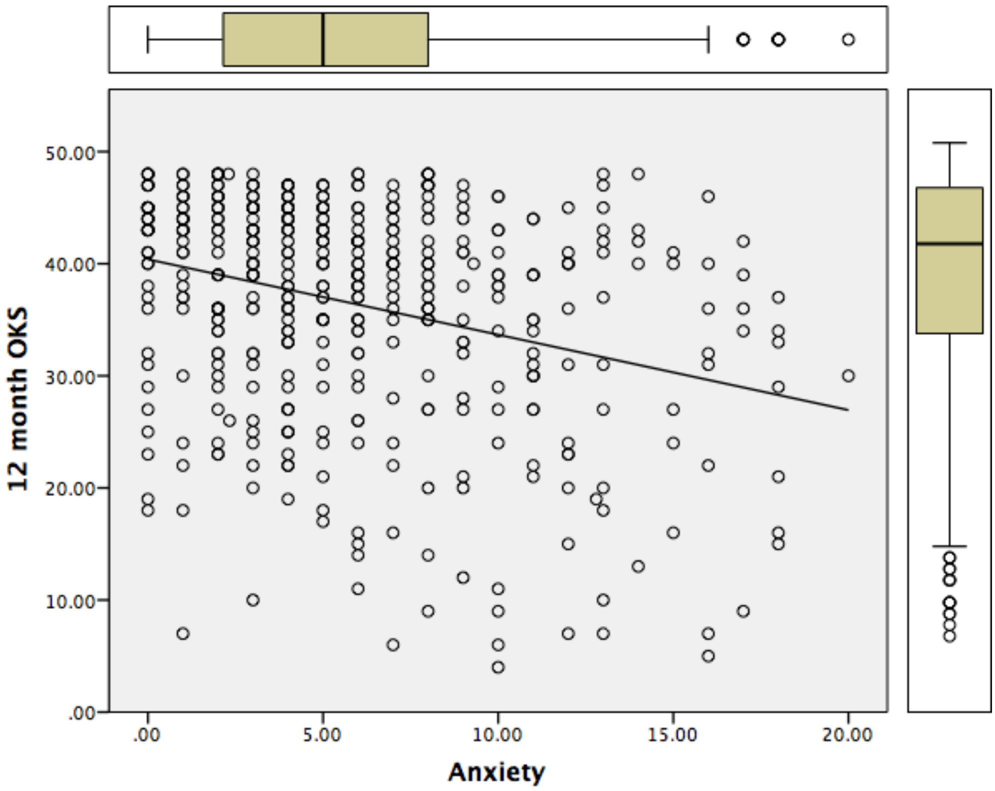

12 month OKS
Helplessness


50.00
40.00
30.00
20.00
10.00
.00
5.00
10.00
15.00
20.00
25.00
12 month OKS
Internality


50.00
40.00
30.00
20.00
10.00
.00
.00
10.00
20.00
30.00
40.00
50.00
60.00
12 month OKS
PCS

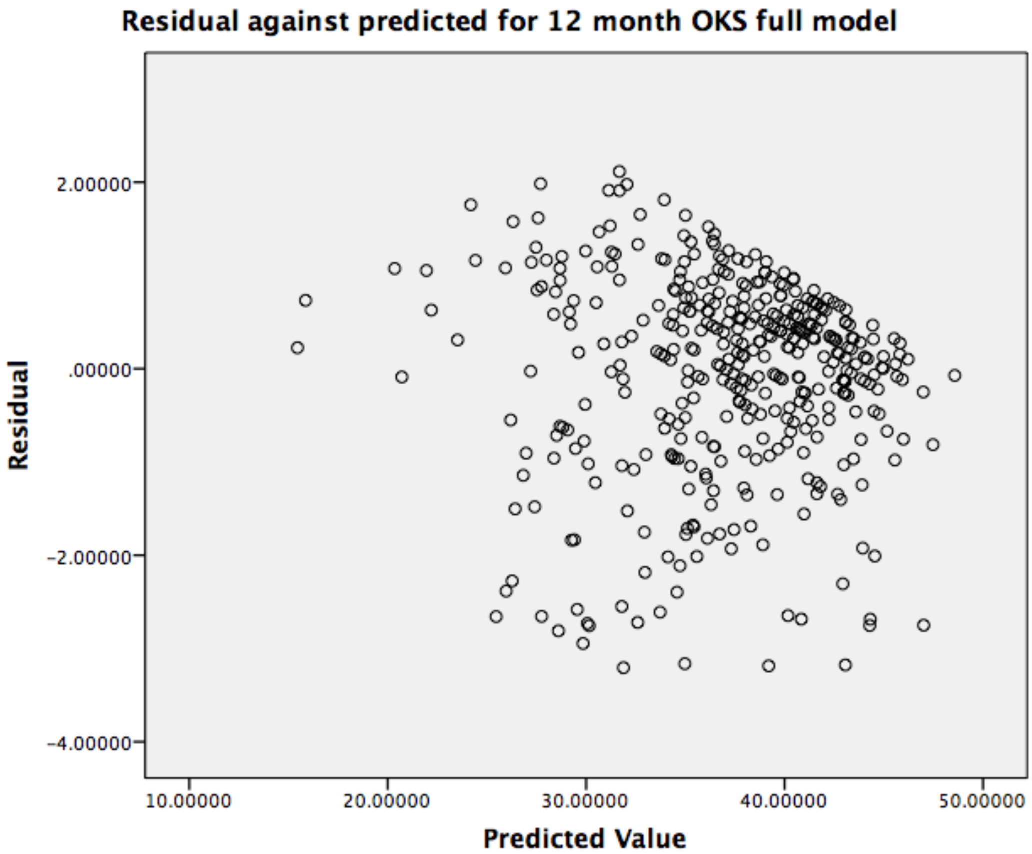

50.00
40.00
30.00
20.00
10.00
.00
12 month OKS
20.00
40.00
60.00
80.00
MCS


50.00
40.00
30.00
20.00
10.00
.00
12 month OKS
.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00
Depression



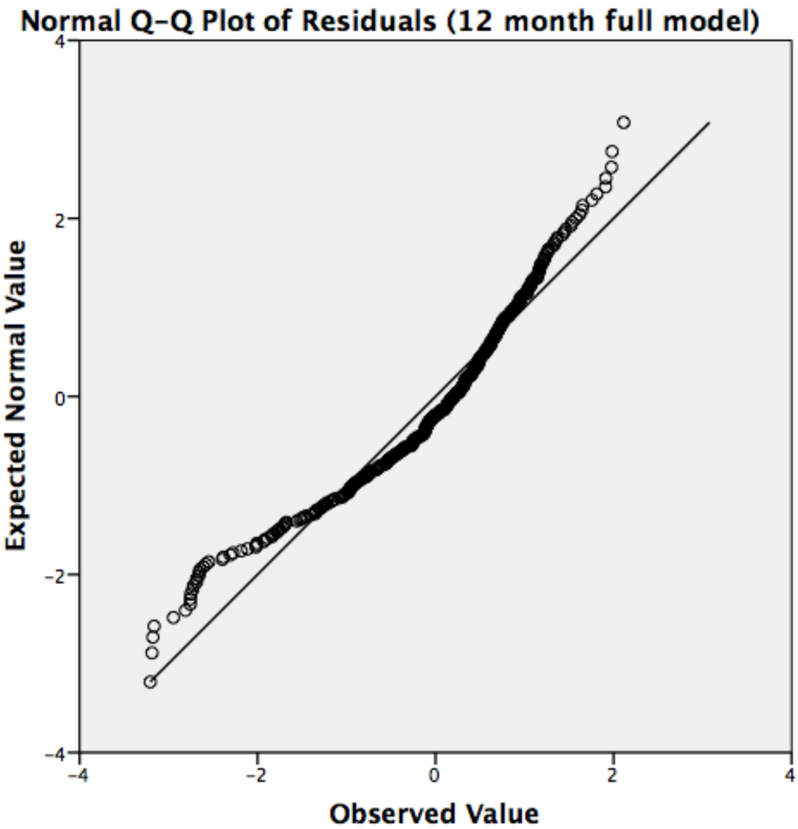
Homoscedasticity

This was tested using a residual versus prediction scatterplot. An even spread of residual values across the range of predicted values suggests heteroscedasticity and linearity.



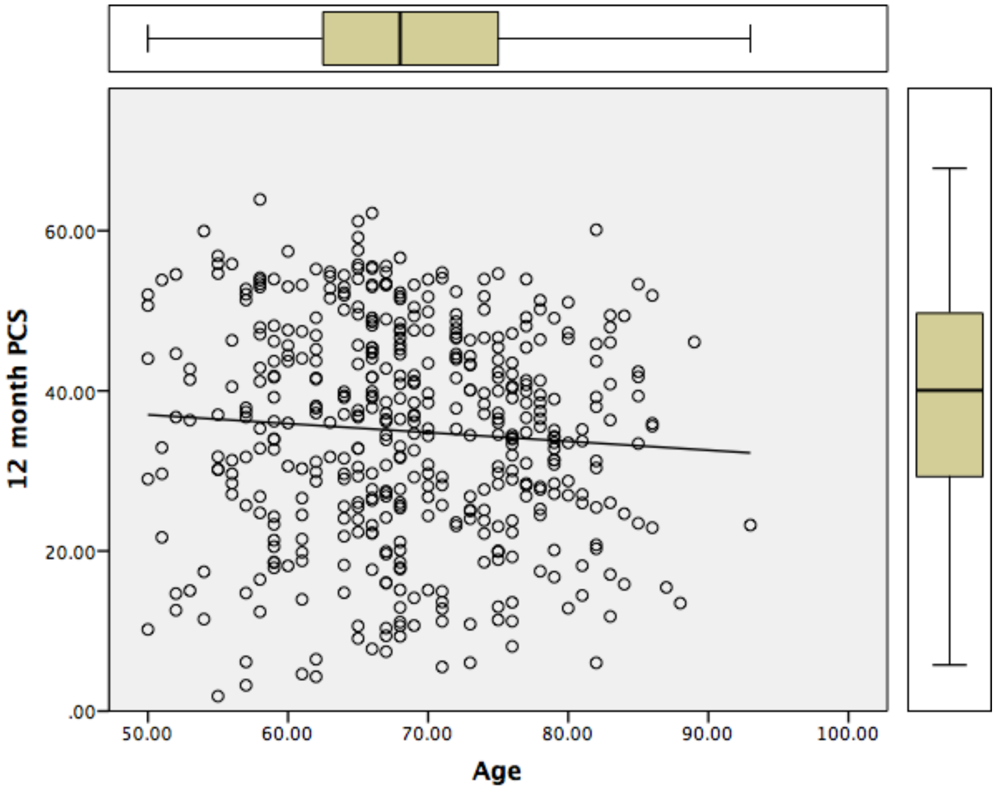
Normality of residuals

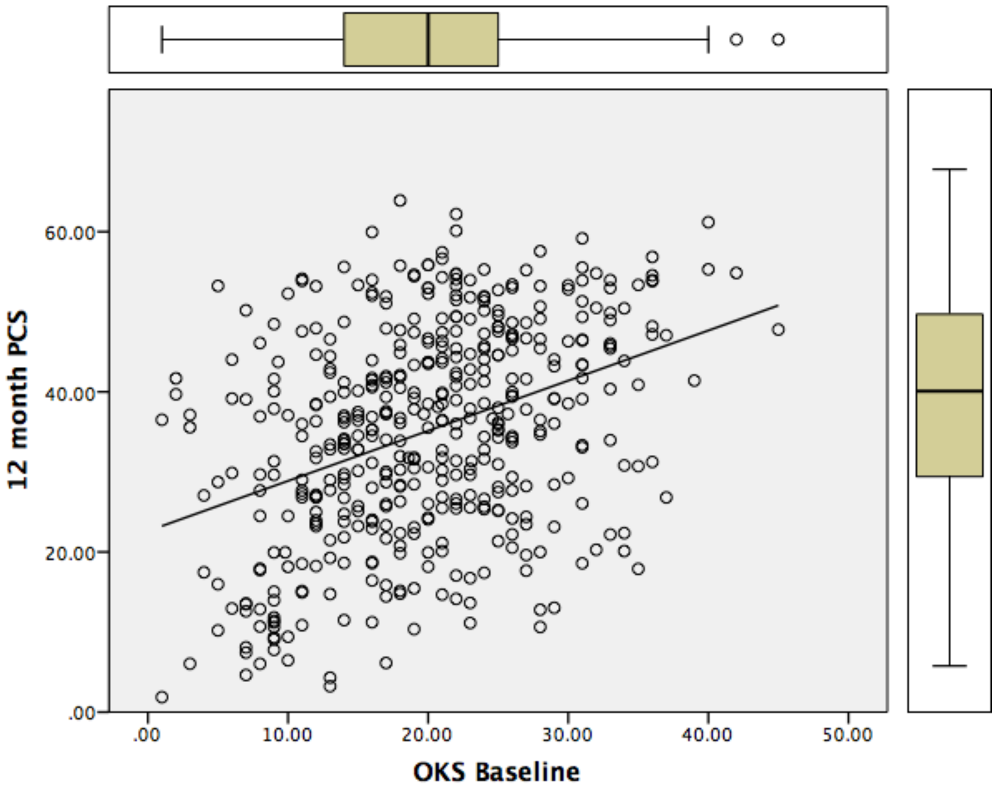
Normality of residuals was assessed informally using a QQ plot:


Normal Q-Q Plot of Residuals (12 month full model)
Expected Normal Value
Observed Value
4
2
0
-2
-4
-4
-2
0
2
4

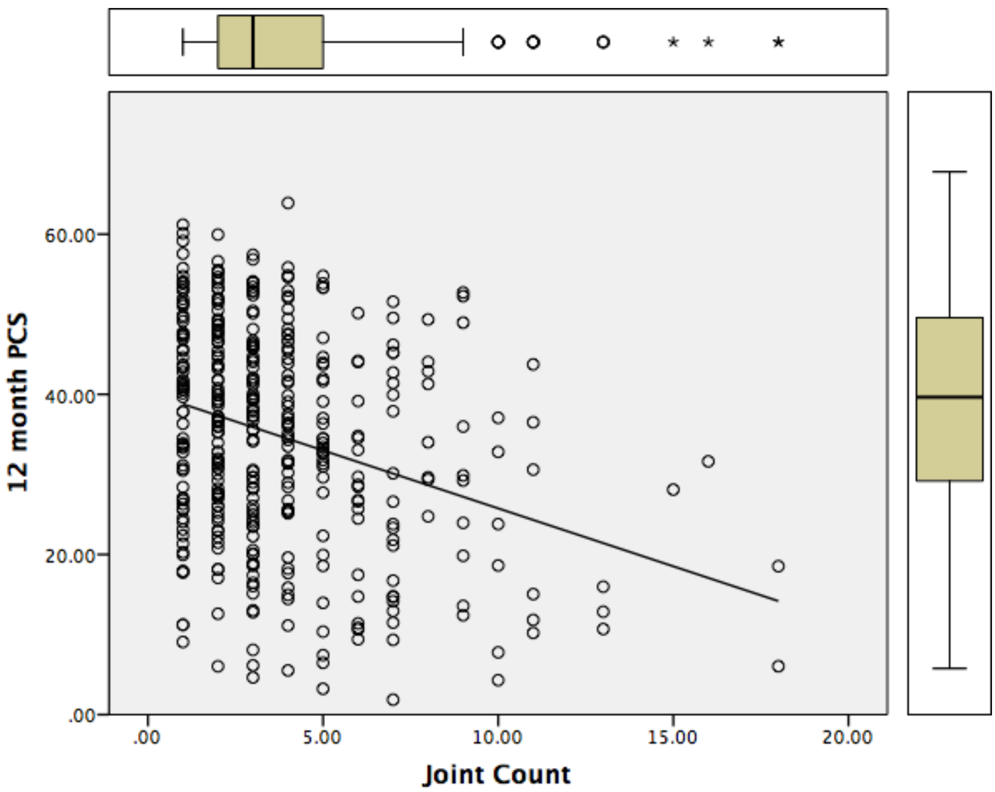
12 month PCS

Scatterplots of each explanatory variable against each scale response variable is plotted below:

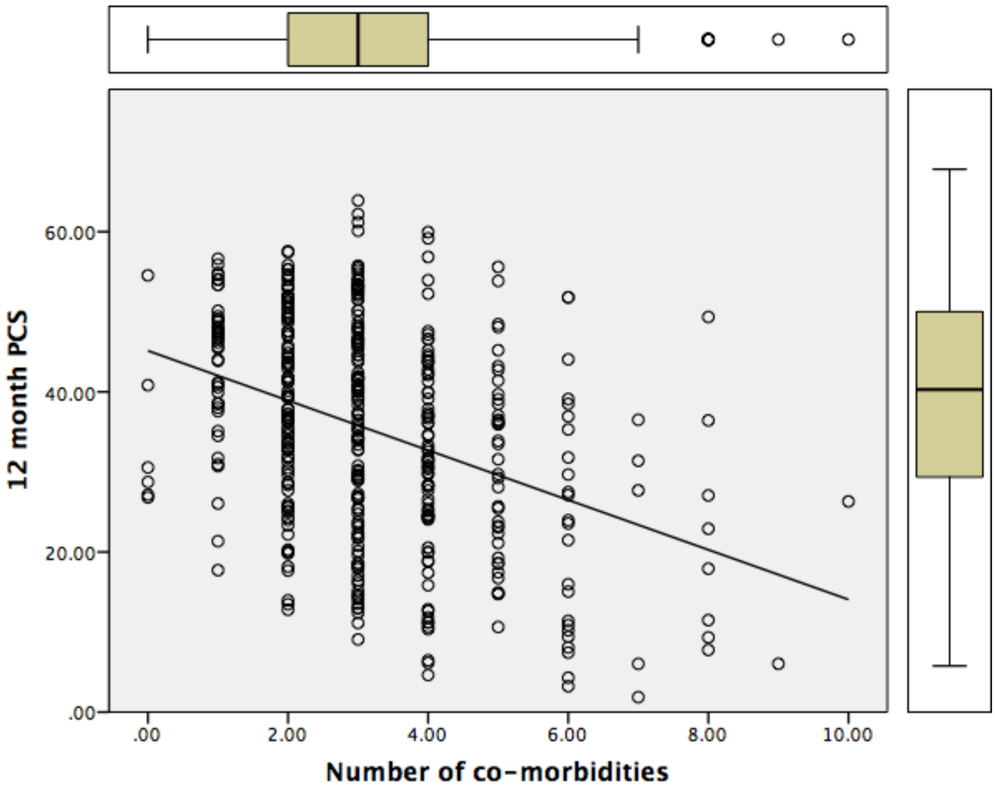




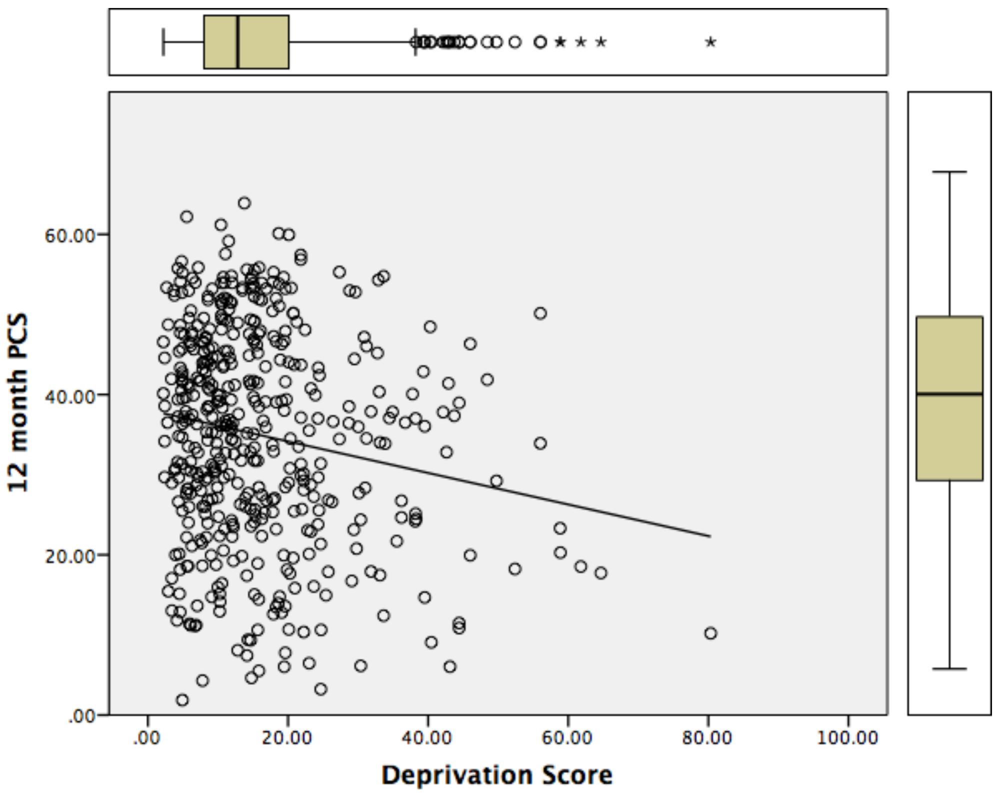
60.00
40.00
20.00
.00
12 month PCS
.00
10.00
20.00
30.00
40.00
50.00
OKS Baseline



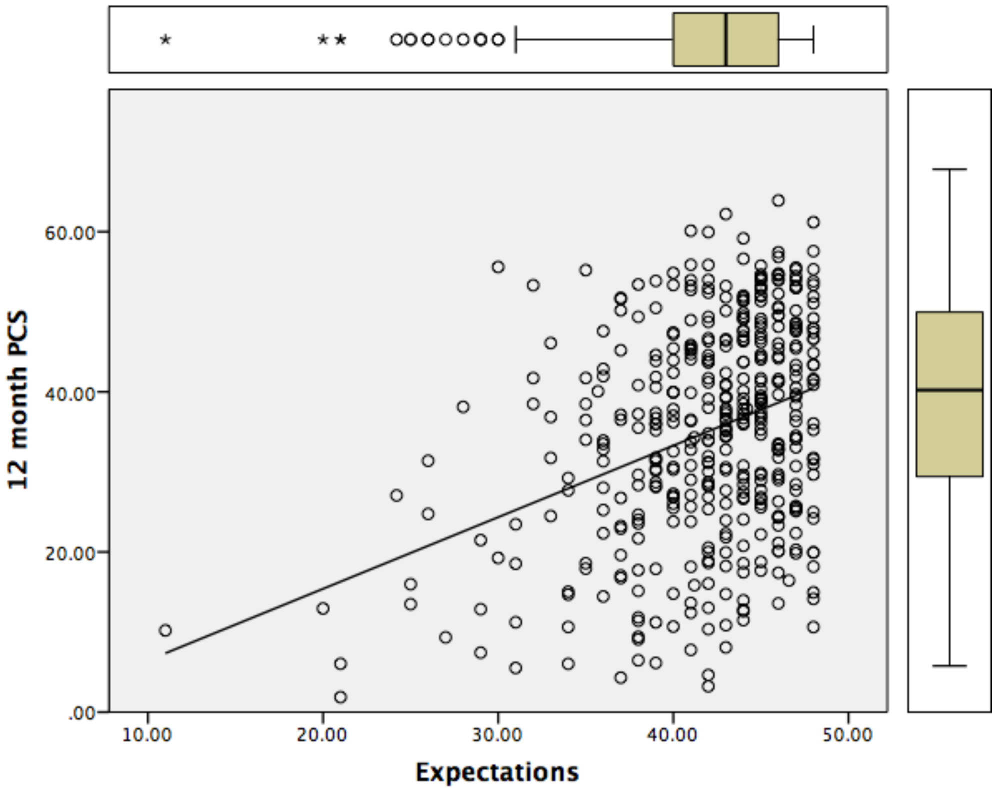
60.00
40.00
20.00
.00
12 month PCS
.00
5.00
10.00
15.00
20.00
Joint Count

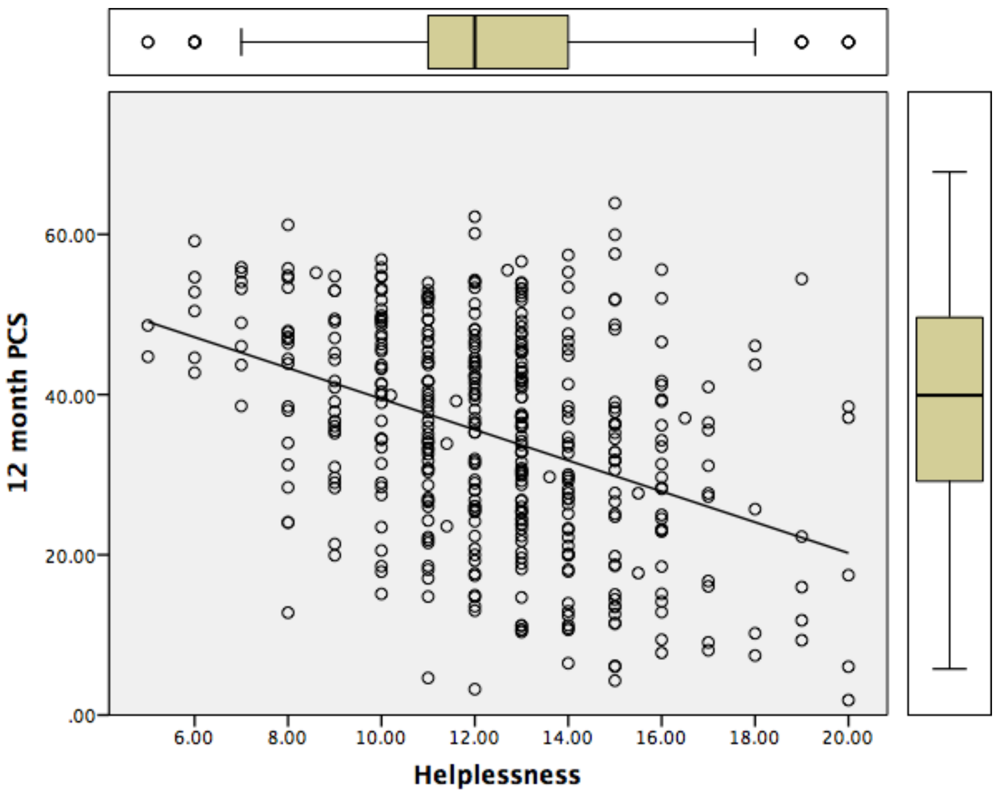


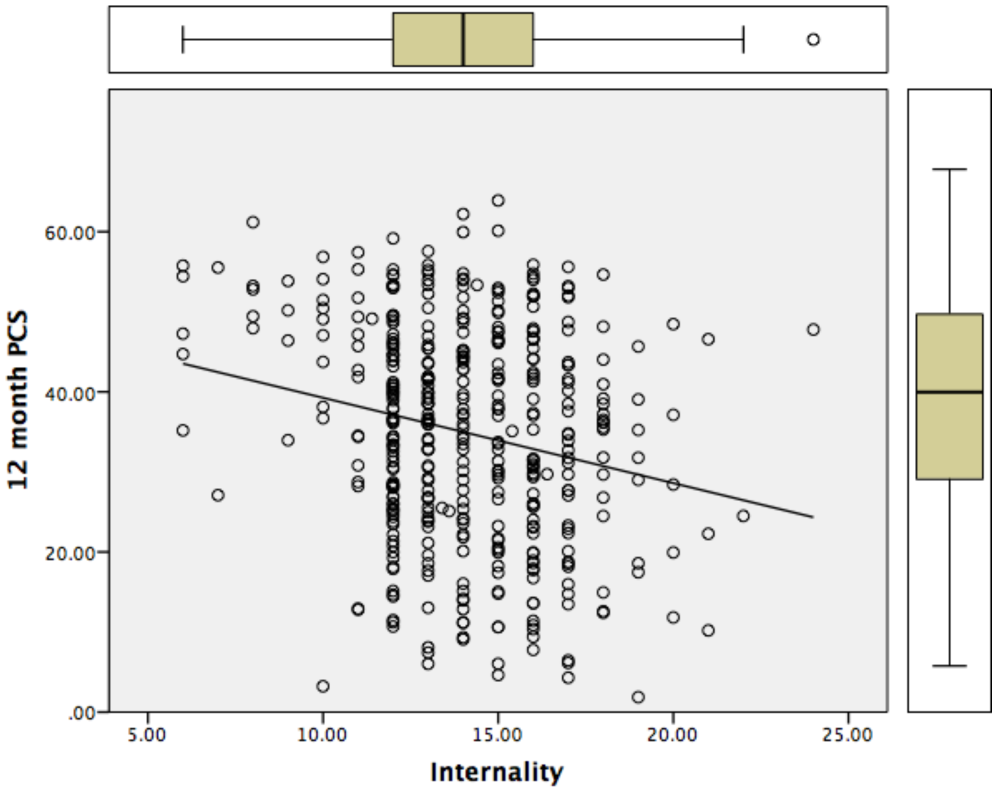
60.00
40.00
20.00
.00
12 month PCS
.00
2.00
4.00
6.00
8.00
10.00
Number of co-morbidities

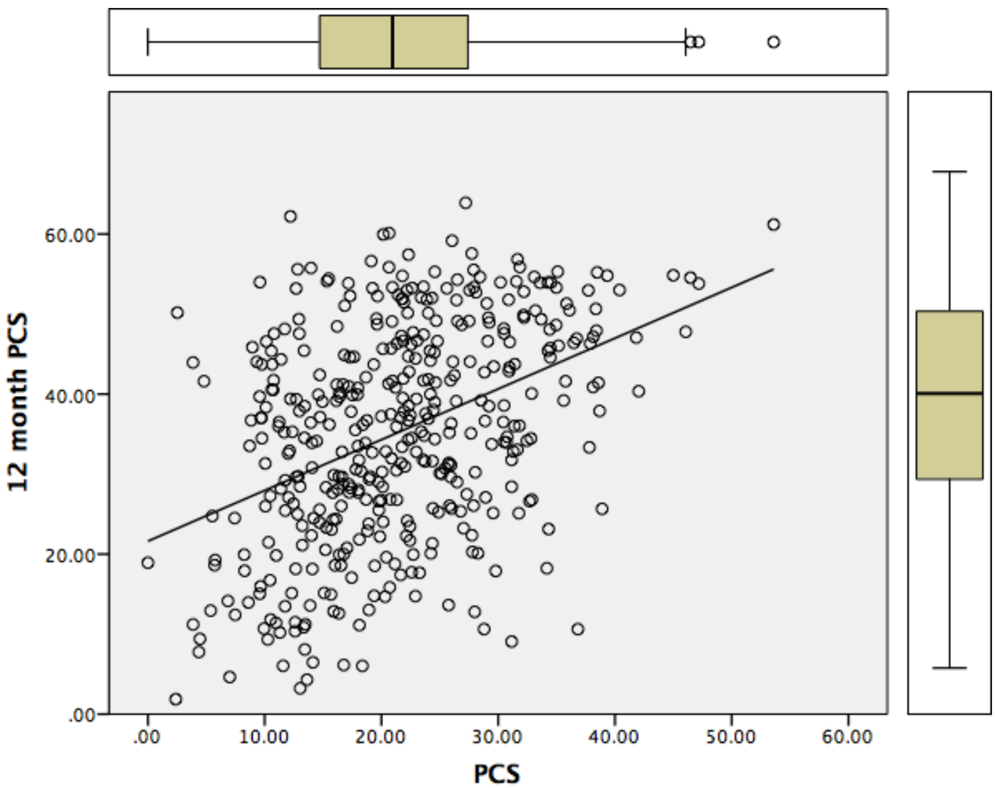


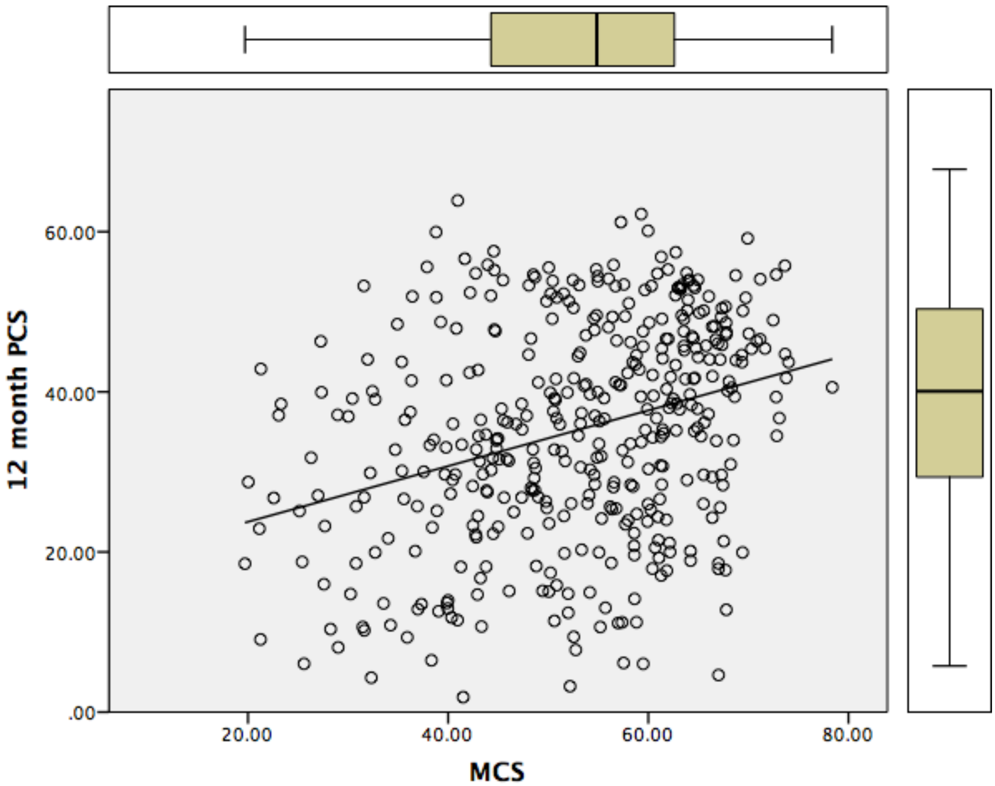
60.00
40.00
20.00
.00
12 month PCS
.00
20.00
40.00
60.00
80.00
100.00
Deprivation Score

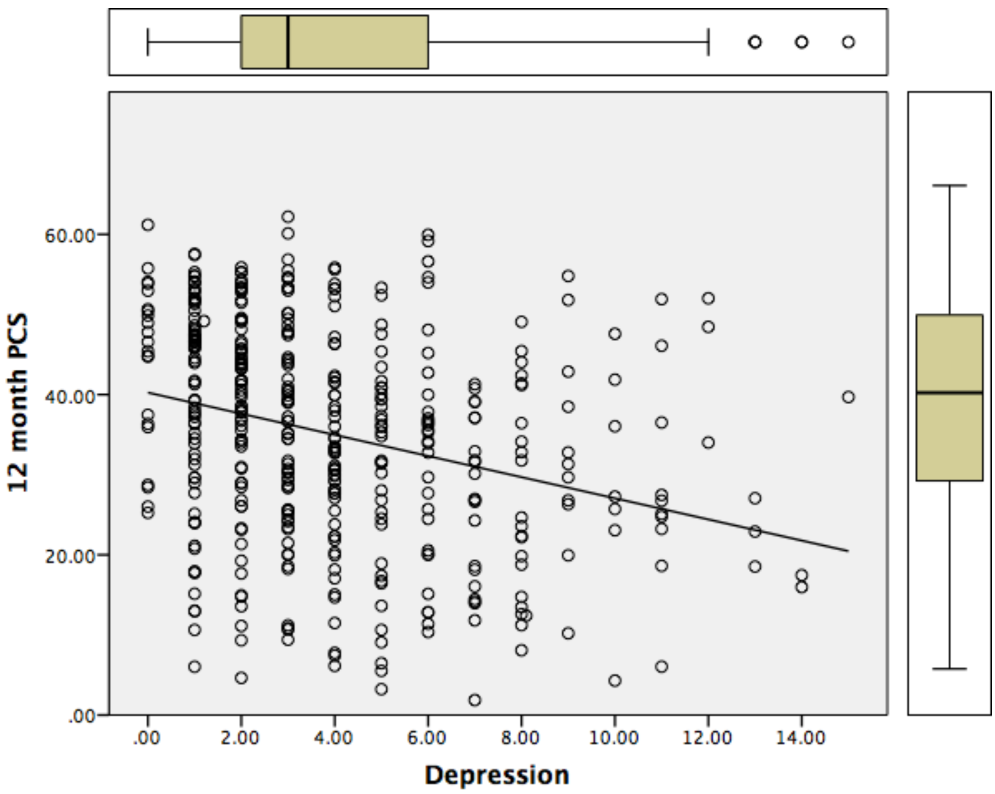

12 month PCS
Expectations
60.00
40.00
20.00
.00
10.00
20.00
30.00
40.00
50.00

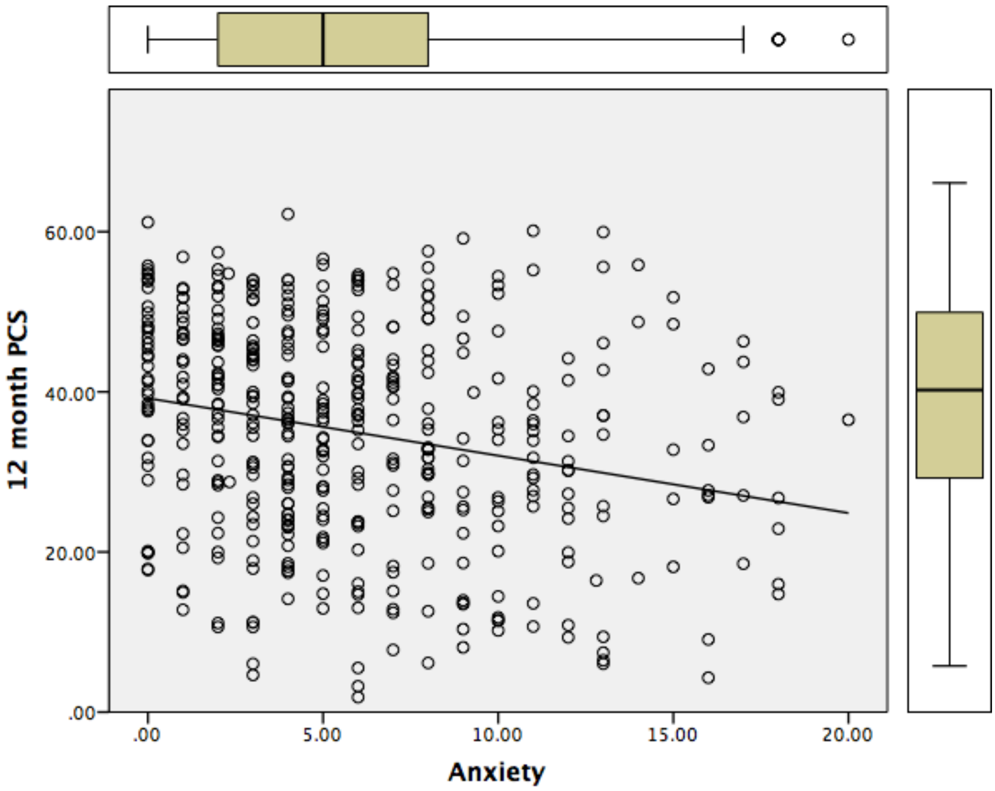

12 month PCS
Helplessness
60.00
40.00
20.00
.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00
20.00


12 month PCS
60.00
40.00
20.00
.00
5.00
10.00
15.00
20.00
25.00
Internality


12 month PCS
60.00
40.00
20.00
.00
.00
10.00
20.00
30.00
40.00
50.00
60.00
PCS

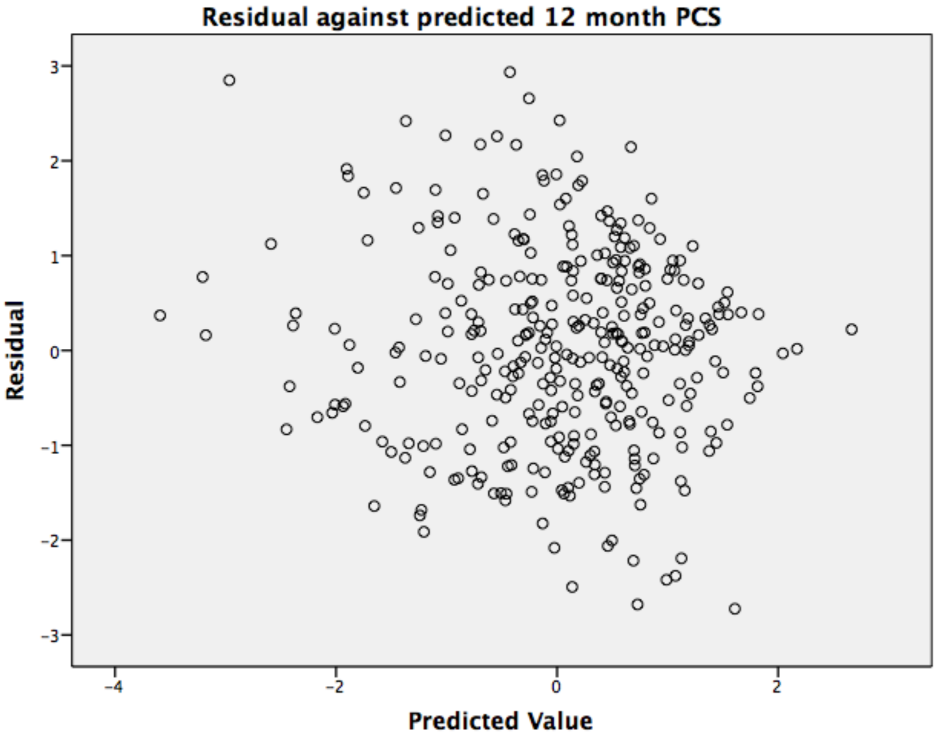

12 month PCS
60.00
40.00
20.00
.00
20.00
40.00
60.00
80.00
MCS


12 month PCS
60.00
40.00
20.00
.00
.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00
Depression



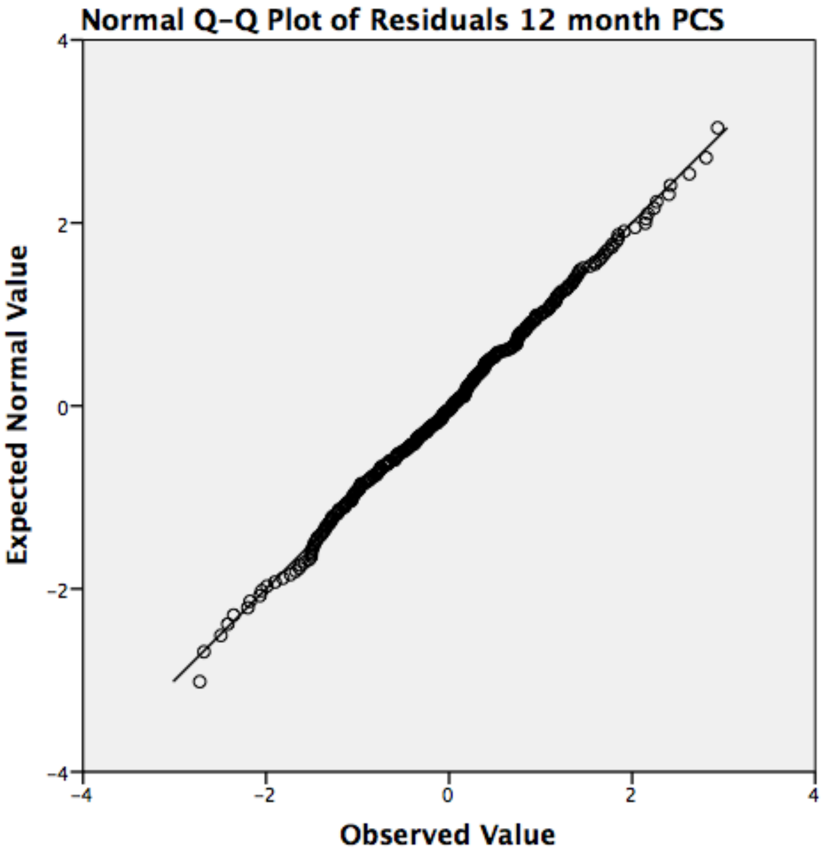
Homoscedasticity

This was tested using a residual versus prediction scatterplot. An even spread of residual values across the range of predicted values suggests heteroscedasticity and linearity.



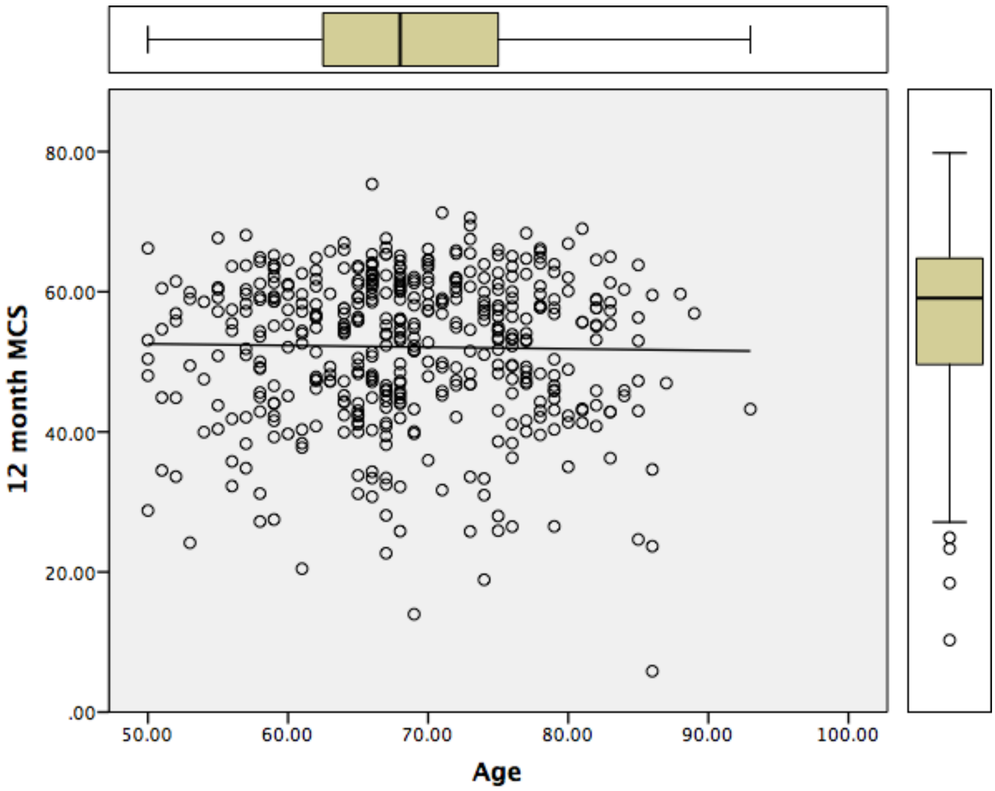
Normality of residuals

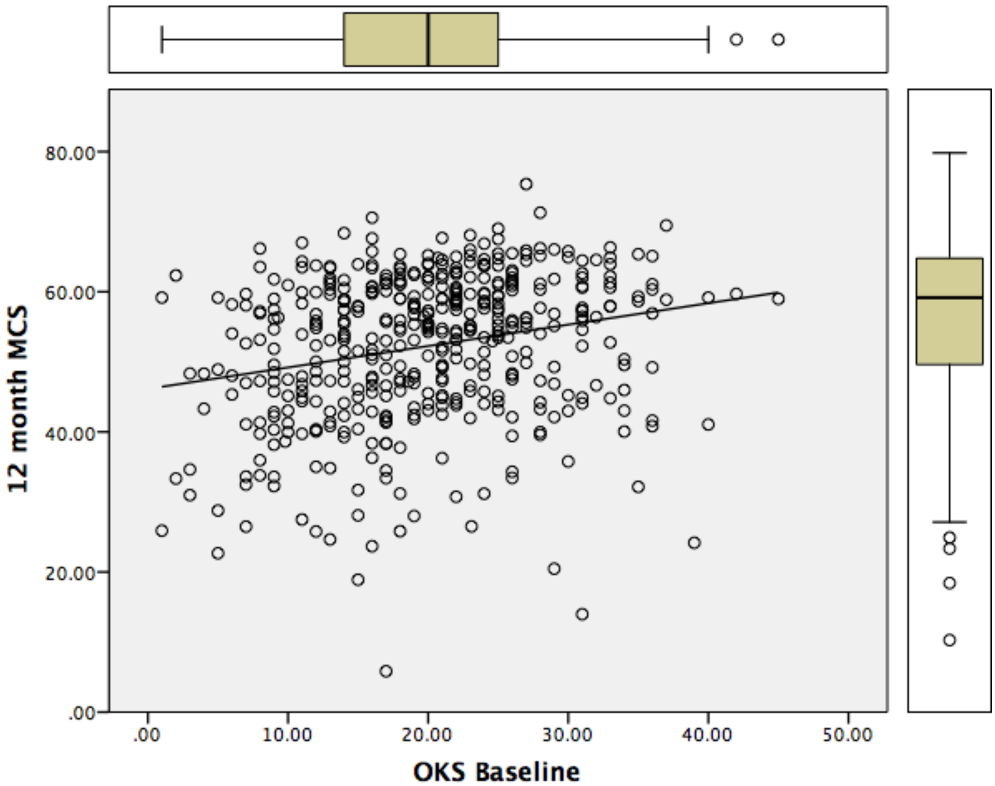
Normality of residuals was assed informally using QQ plots:

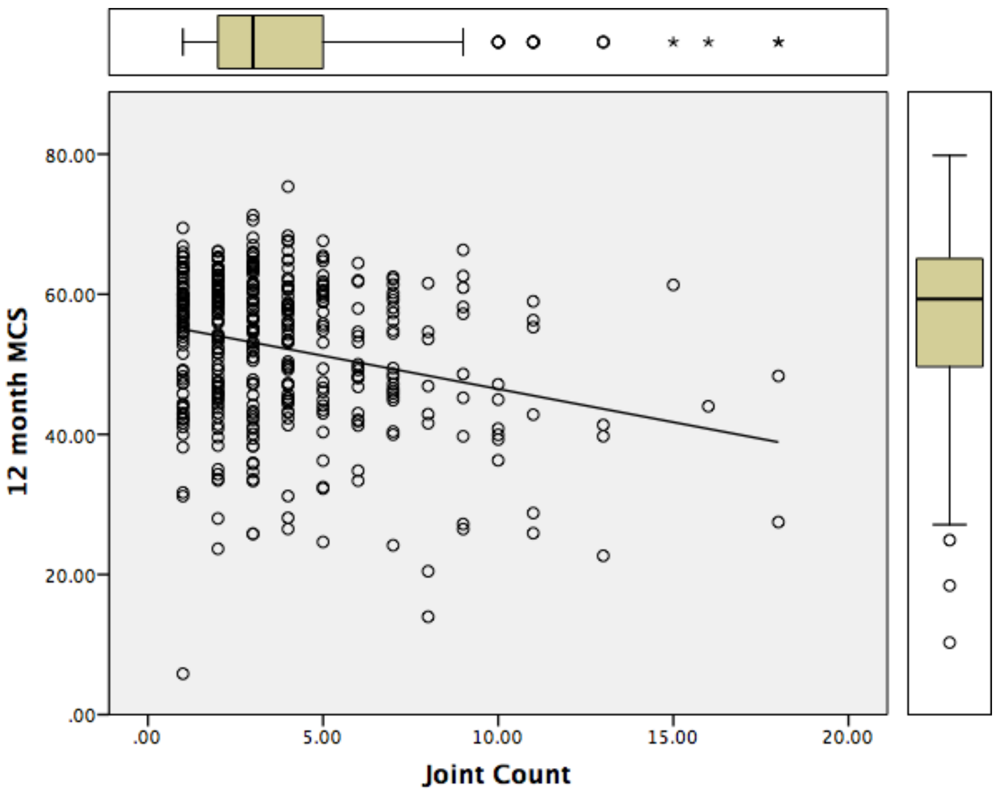

Normal Q-Q Plot of Residuals 12 month PCS
Expected Normal Value
Observed Value
4
2
0
-2
-4
-4
-2
0
2
4

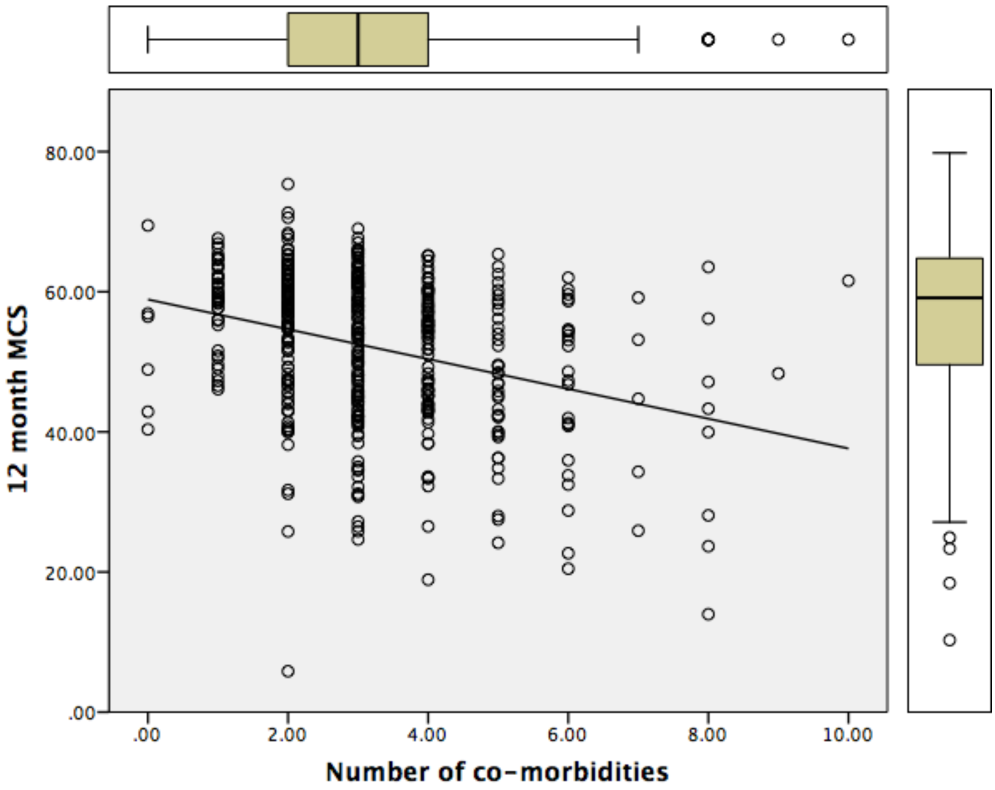
12 Month MCS

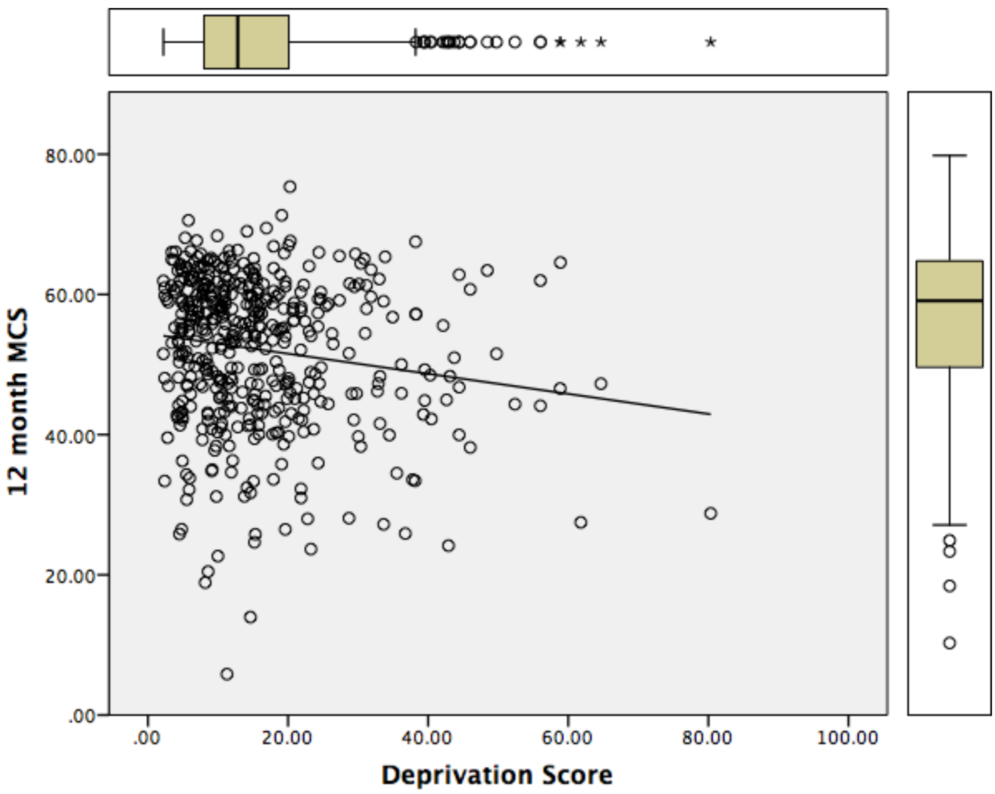
Scatterplots of each explanatory variable against each scale response variable is plotted below:

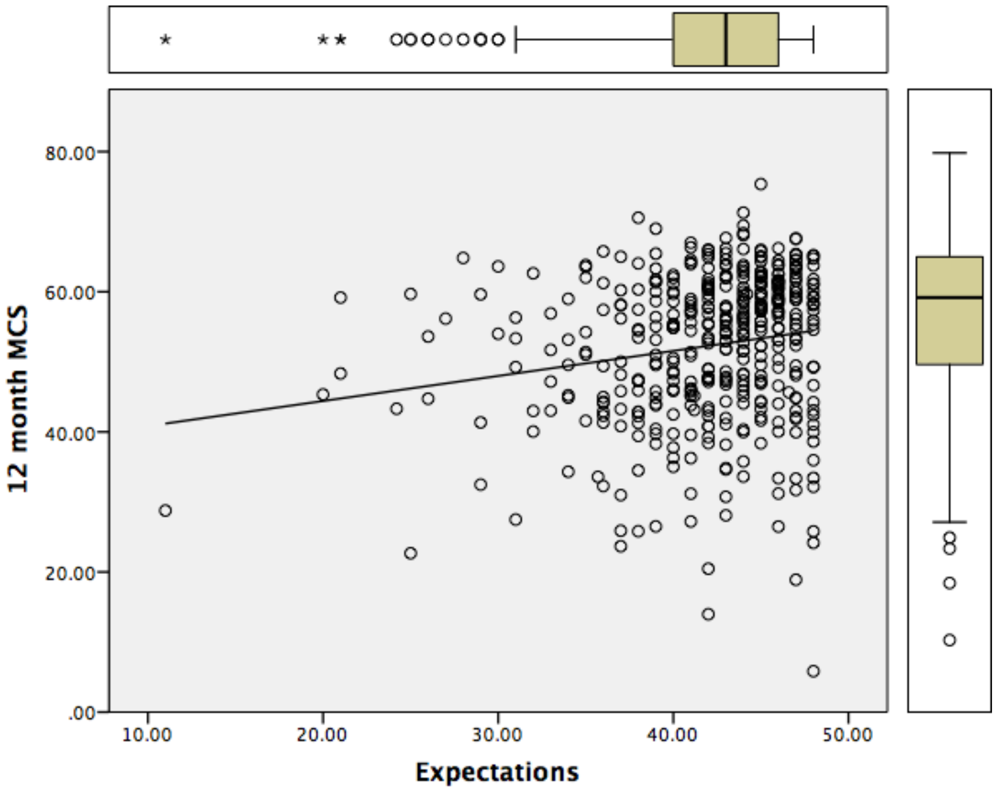



80.00
60.00
40.00
20.00
.00
12 month MCS
.00
10.00
20.00
30.00
40.00
50.00
OKS Baseline

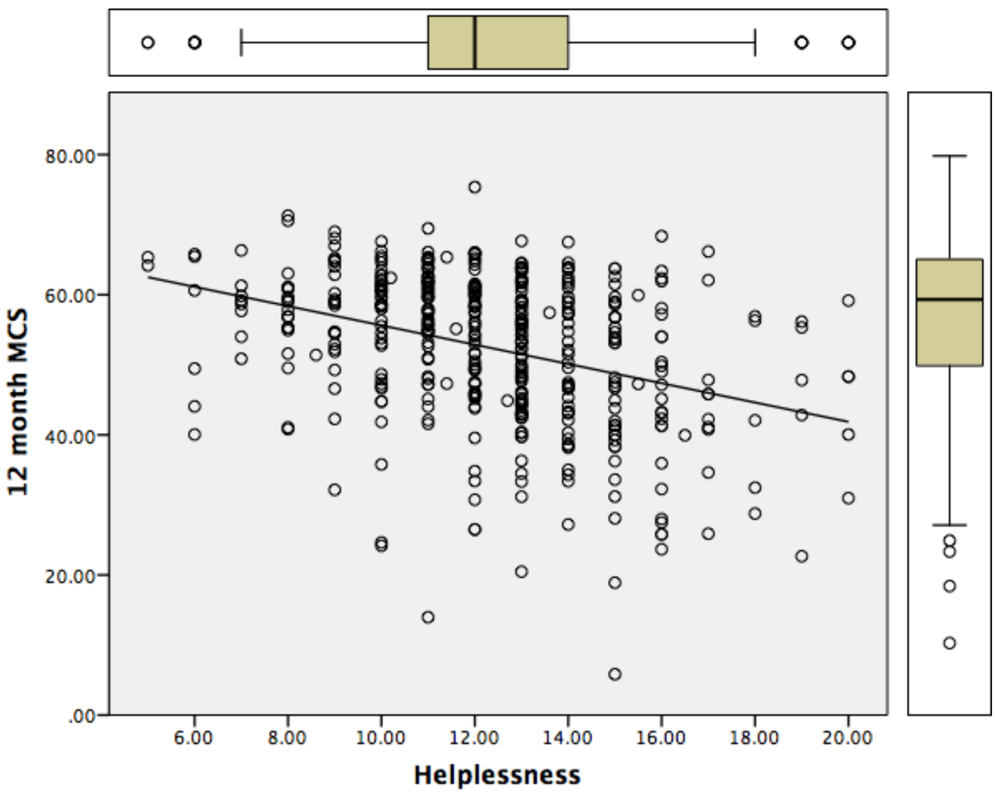

80.00
60.00
40.00
20.00
.00
12 month MCS
.00
5.00
10.00
15.00
20.00
Joint Count


80.00
60.00
40.00
20.00
.00
12 month MCS
.00
2.00
4.00
6.00
8.00
10.00
Number of co-morbidities

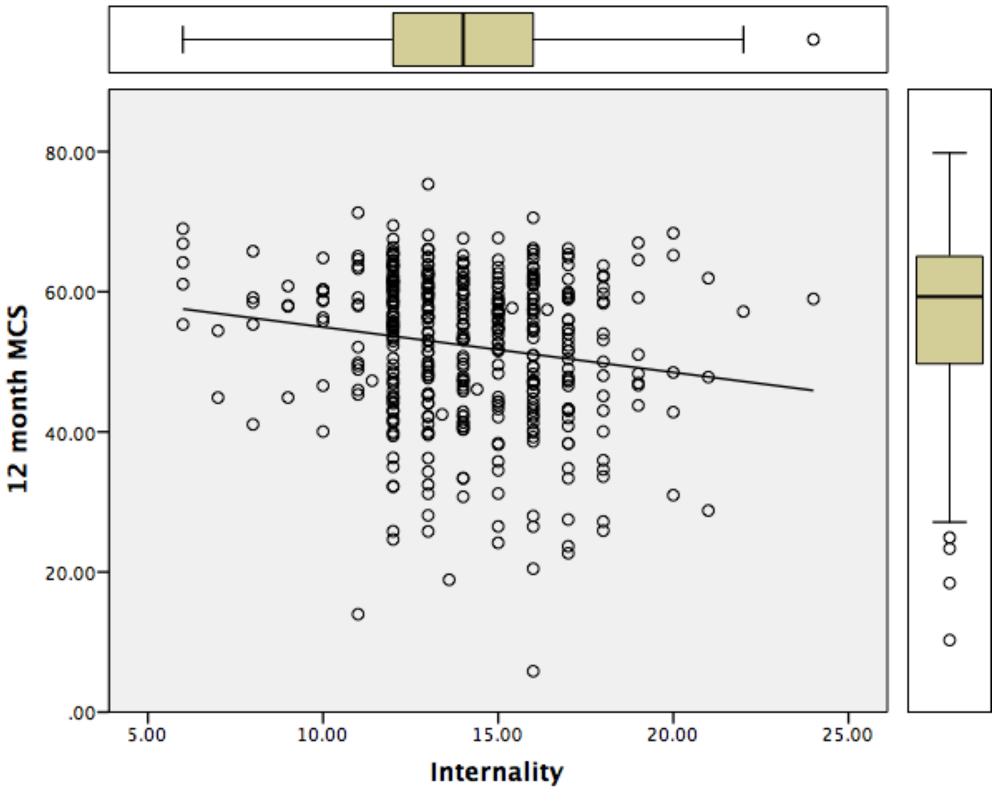

80.00
60.00
40.00
20.00
.00
12 month MCS
.00
20.00
40.00
60.00
80.00
100.00
Deprivation Score

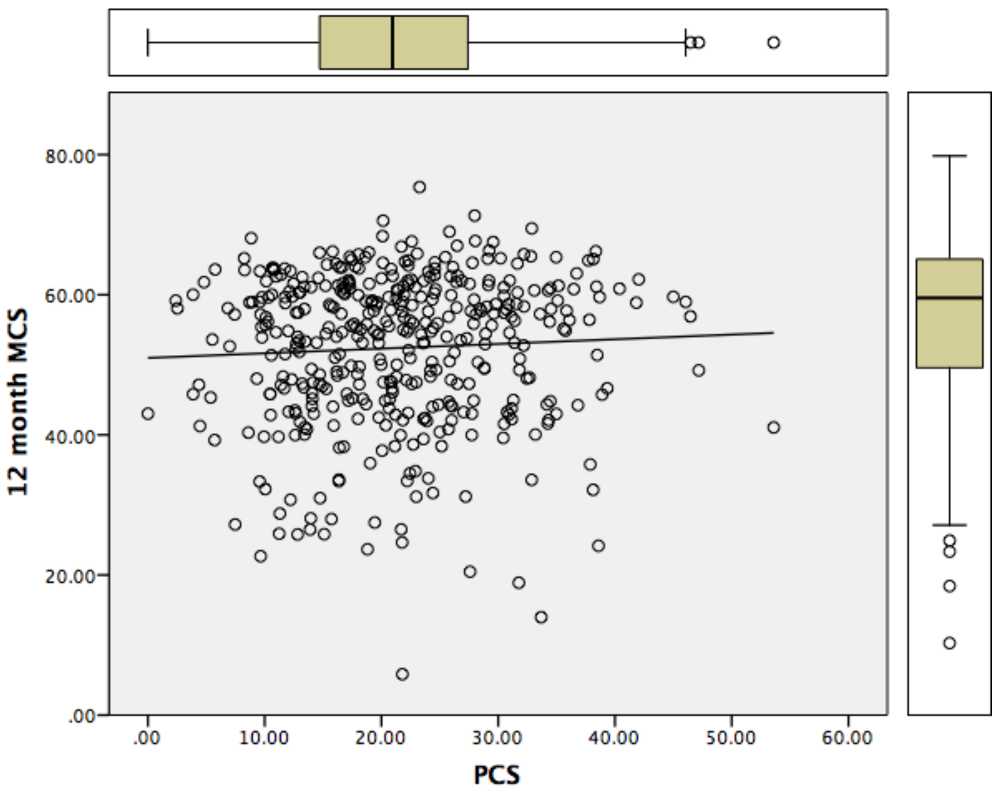


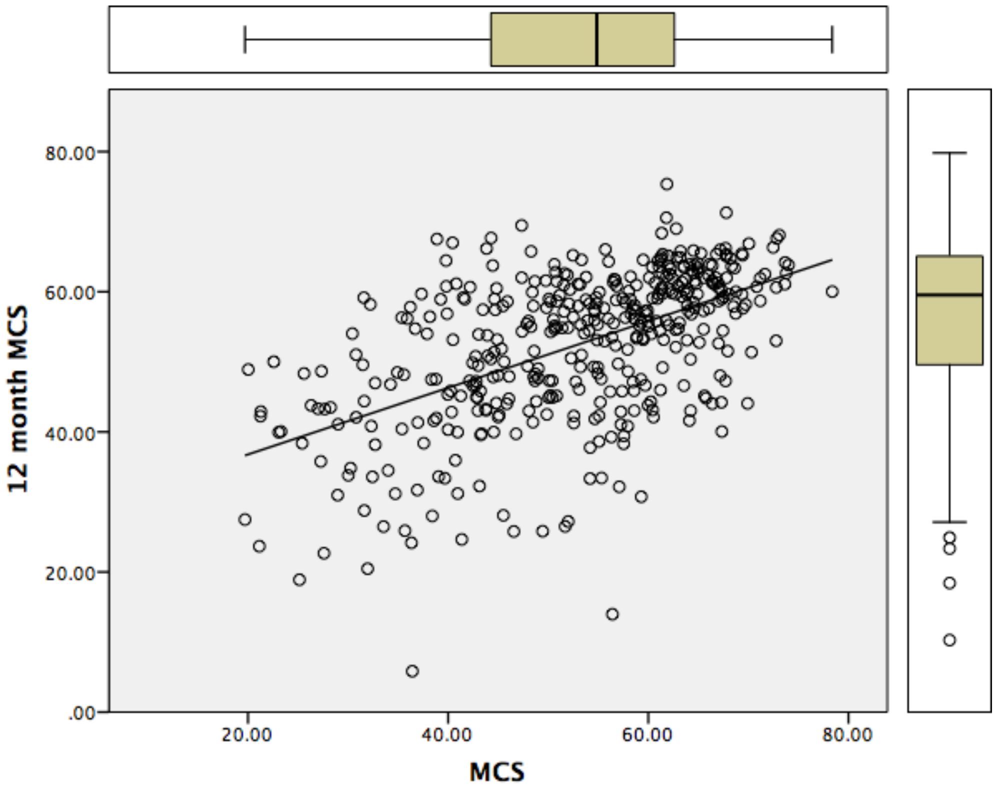
80.00
60.00
40.00
20.00
.00
12 month MCS
10.00
20.00
30.00
40.00
50.00
Expectations

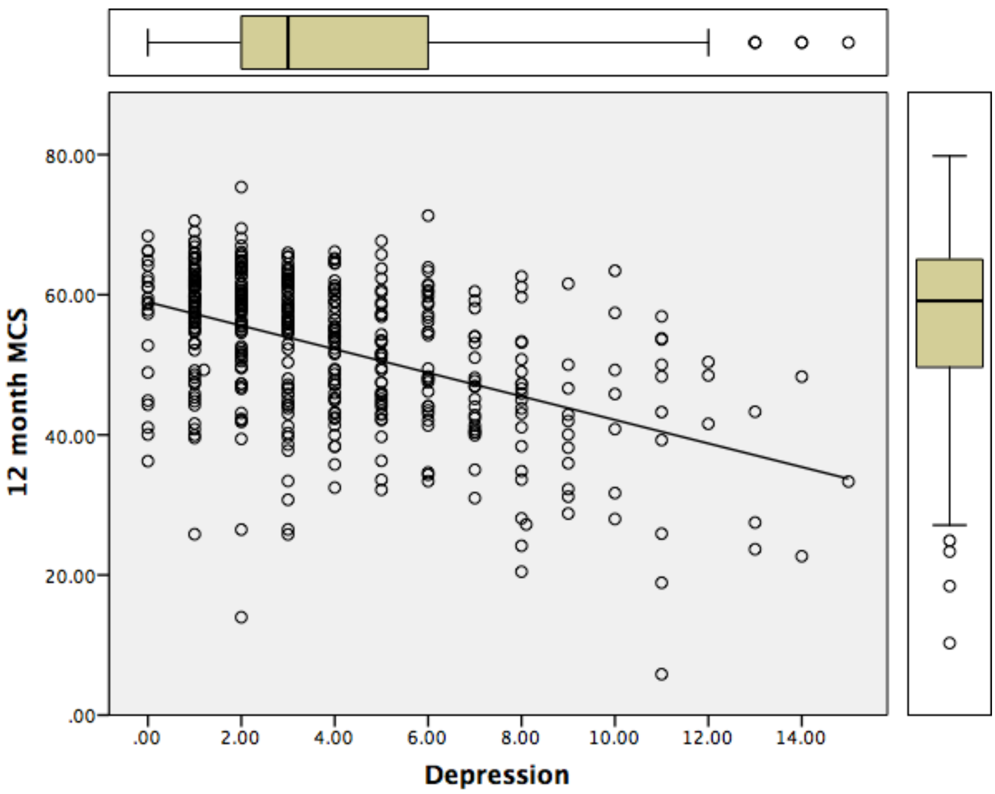


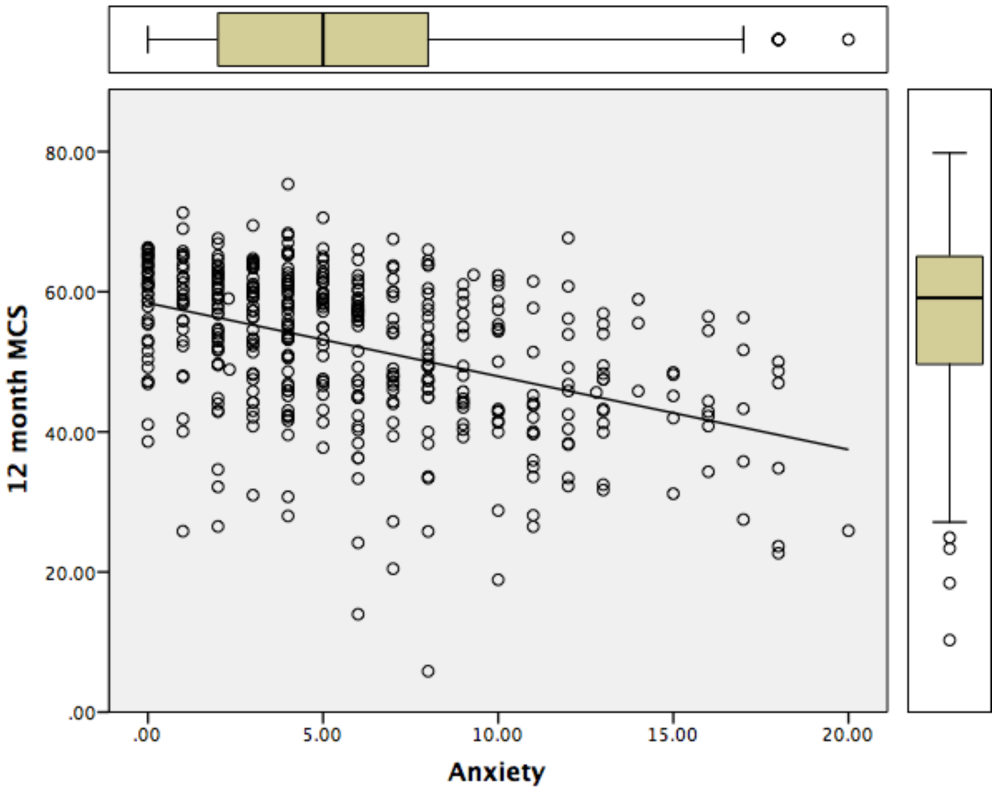
80.00
60.00
40.00
20.00
.00
12 month MCS
6.00
8.00
10.00
12.00
14.00
16.00
18.00
20.00
Helplessness


80.00
60.00
40.00
20.00
.00
12 month MCS
5.00
10.00
15.00
20.00
25.00
Internality


80.00
60.00
40.00
20.00
.00
12 month MCS
.00
10.00
20.00
30.00
40.00
50.00
60.00
PCS

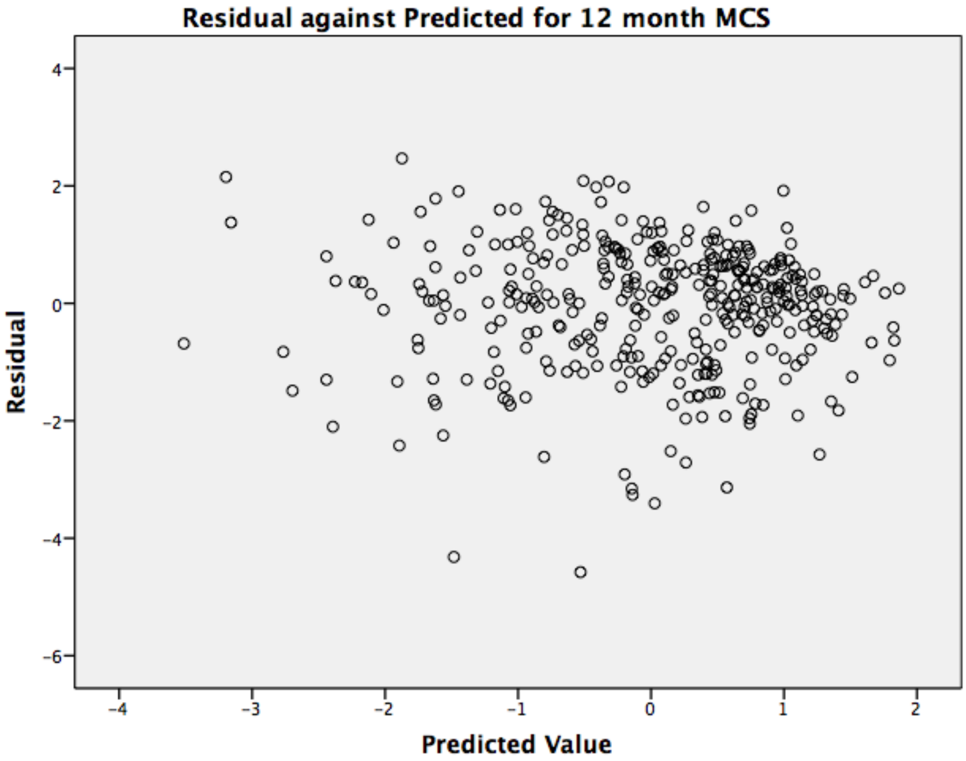

80.00
60.00
40.00
20.00
.00
12 month MCS
20.00
40.00
60.00
80.00
MCS


80.00
60.00
40.00
20.00
.00
12 month MCS
.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00
Depression



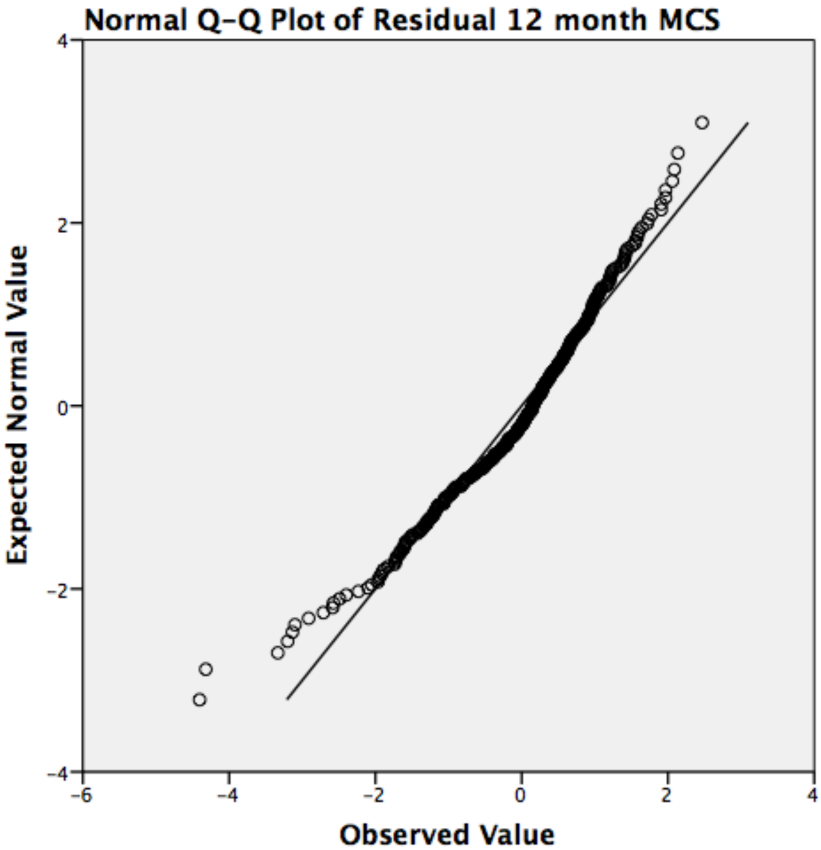
Homoscedasticity

This was tested using a residual versus prediction scatterplot. An even spread of residual values across the range of predicted values suggests heteroscedasticity and linearity.



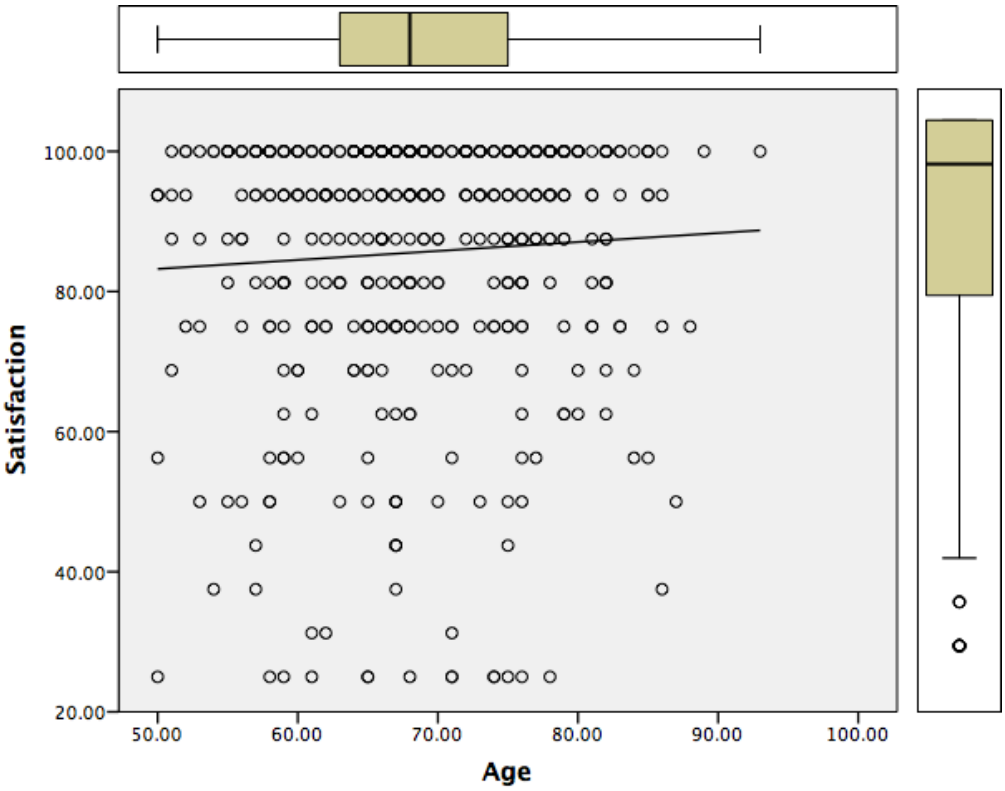
Normality of residuals

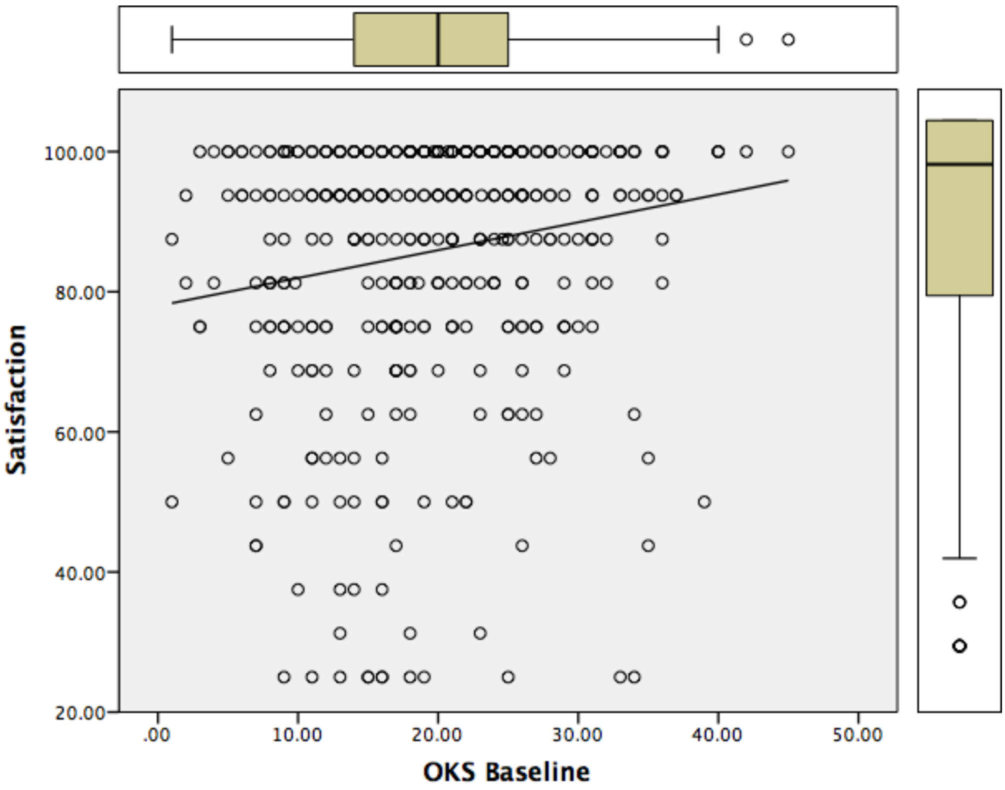
Normality of residuals was assed informally using QQ plots:

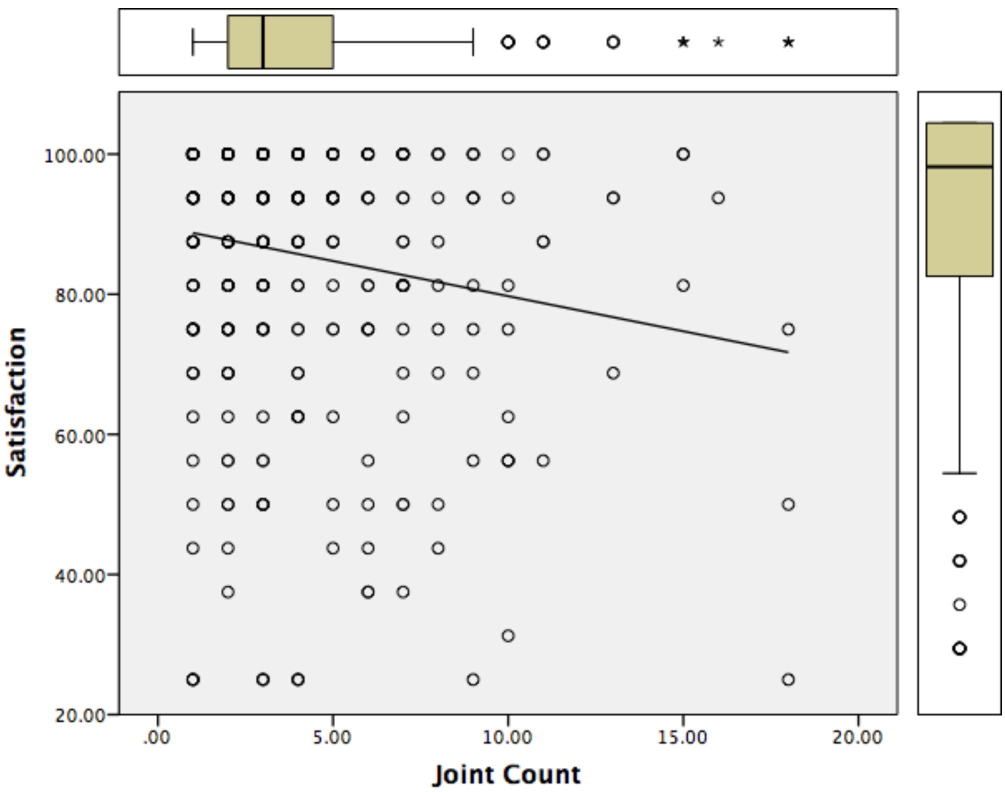

Normal Q-Q Plot of Residual 12 month MCS
Expected Normal Value
Observed Value
4
2
0
-2
-4
-6
-4
-2
0
2
4

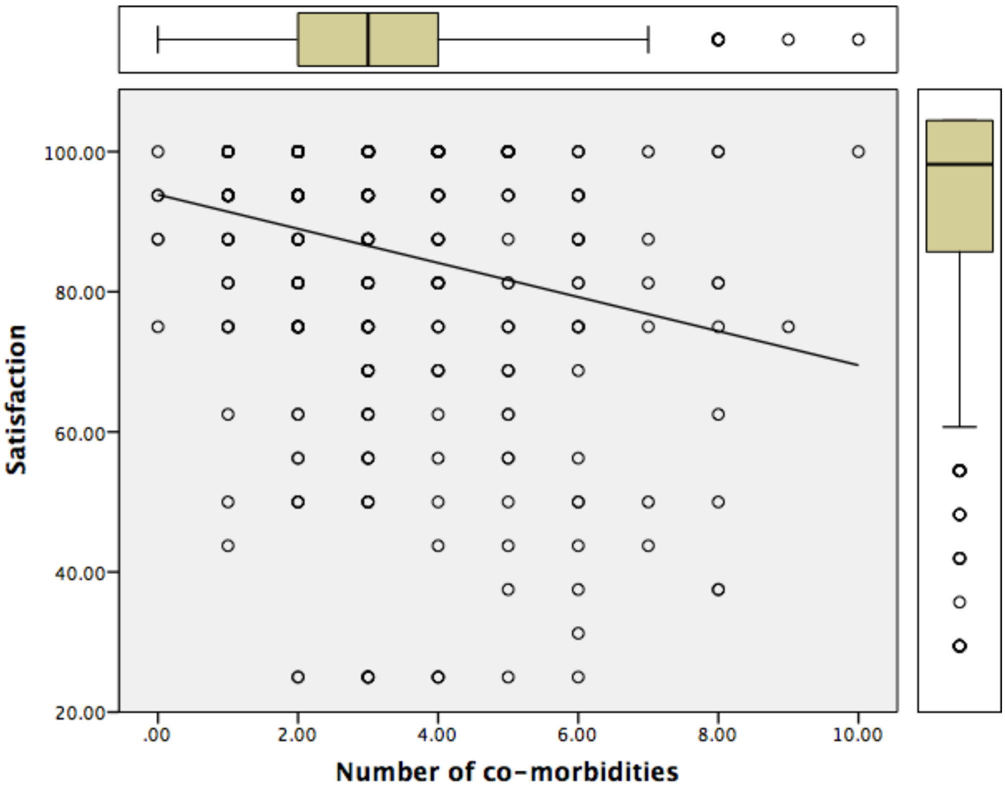
12 month satisfaction

Scatterplots of each explanatory variable against each scale response variable is plotted below:

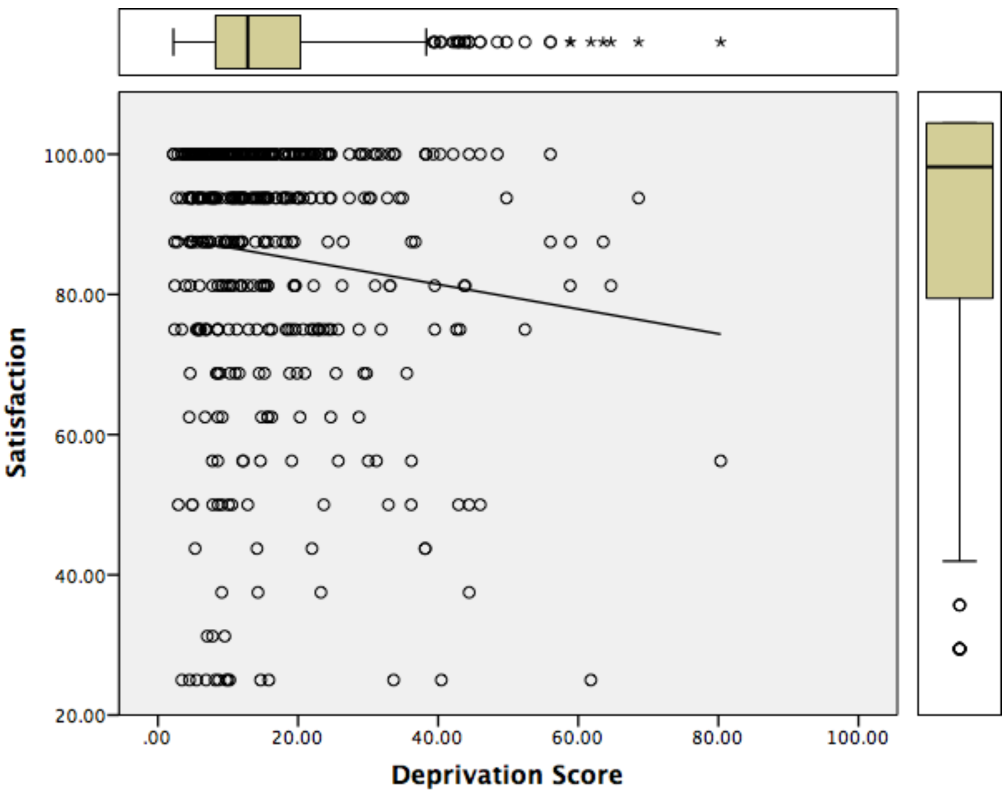



Satisfaction
100.00
80.00
60.00
40.00
20.00
.00
10.00
20.00
30.00
40.00
50.00
OKS Baseline

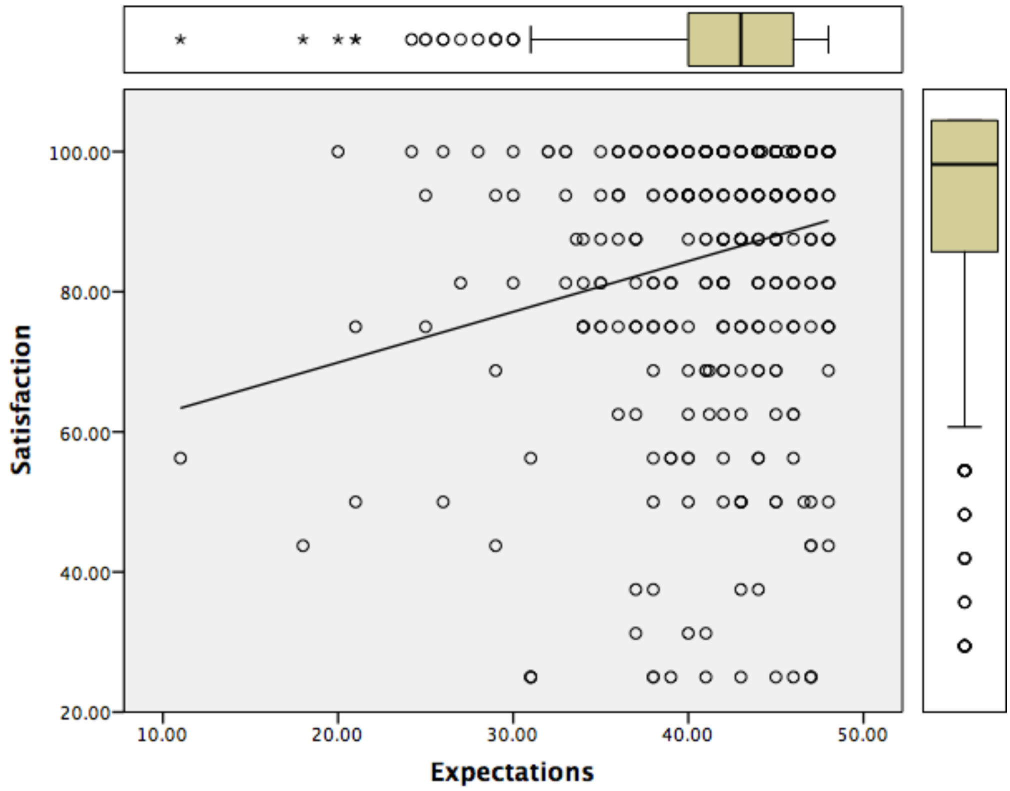

Satisfaction
100.00
80.00
60.00
40.00
20.00
.00
5.00
10.00
15.00
20.00
Joint Count



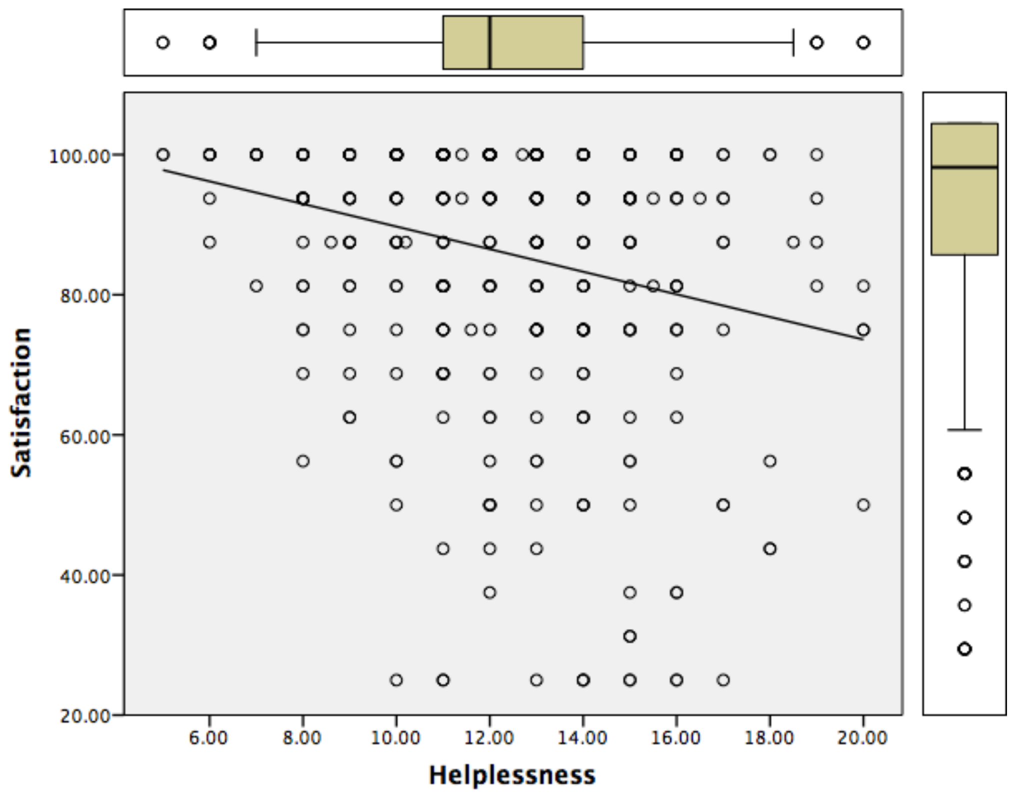
Satisfaction
100.00
80.00
60.00
40.00
20.00
.00
2.00
4.00
6.00
8.00
10.00
Number of co-morbidities



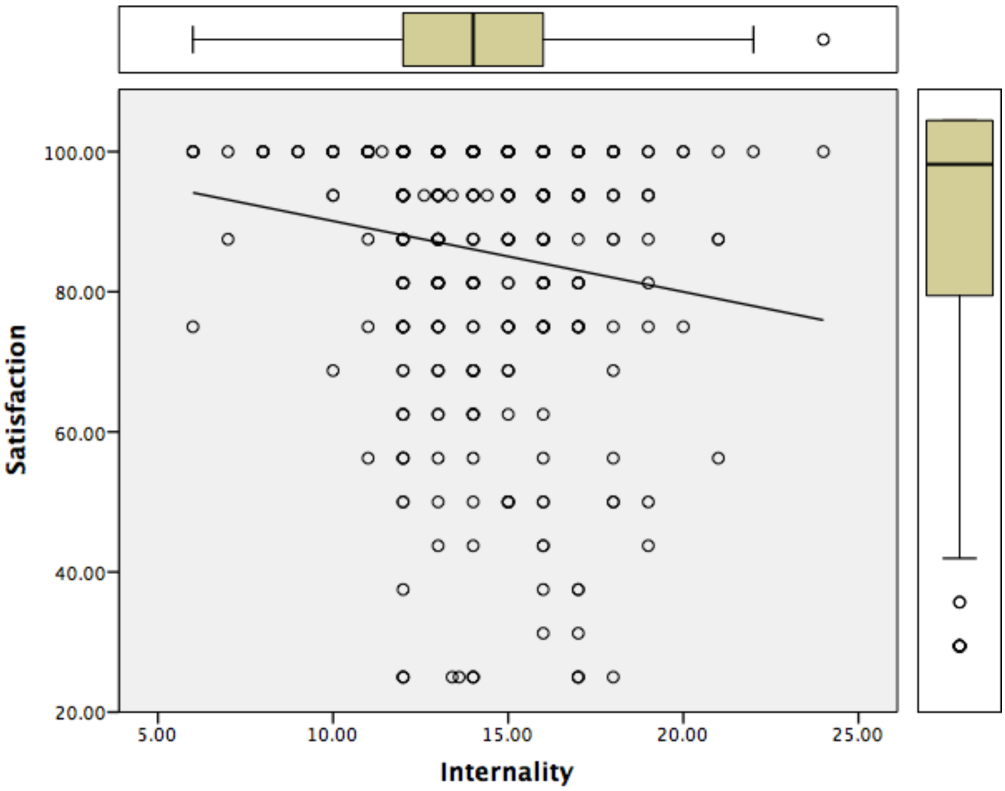
Satisfaction
100.00
80.00
60.00
40.00
20.00
.00
20.00
40.00
60.00
80.00
100.00
Deprivation Score



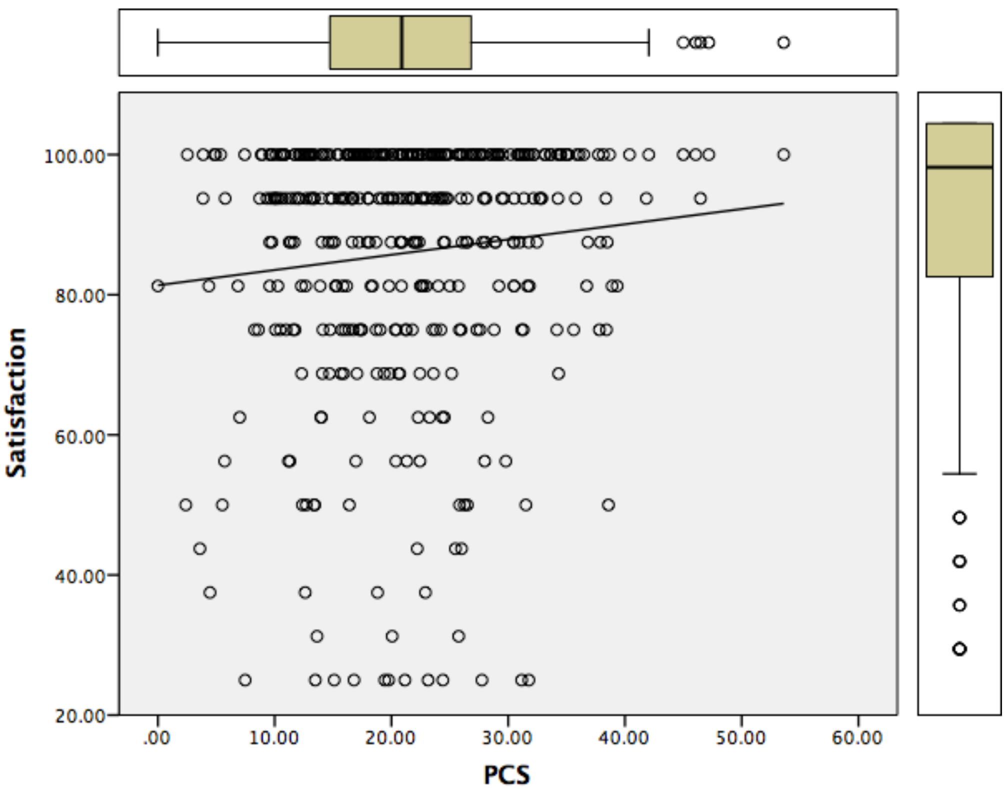
100.00
80.00
60.00
40.00
20.00
Satisfaction
10.00
20.00
30.00
40.00
50.00
Expectations



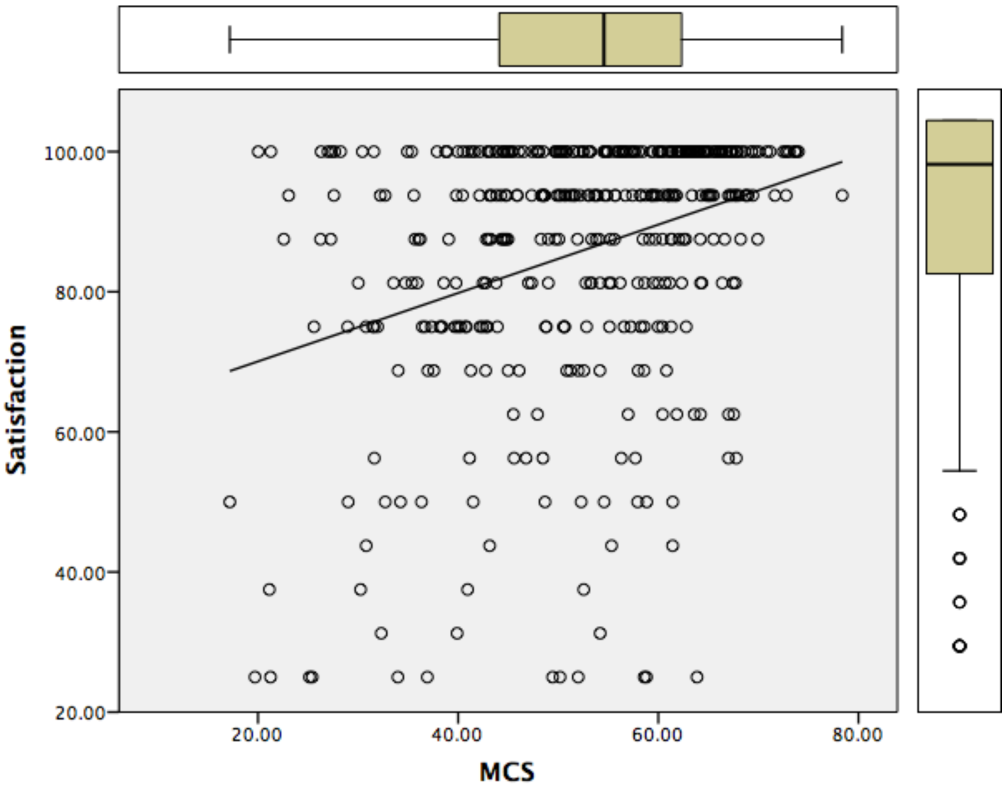
100.00
80.00
60.00
40.00
20.00
Satisfaction
6.00
8.00
10.00
12.00
14.00
16.00
18.00
20.00
Helplessness

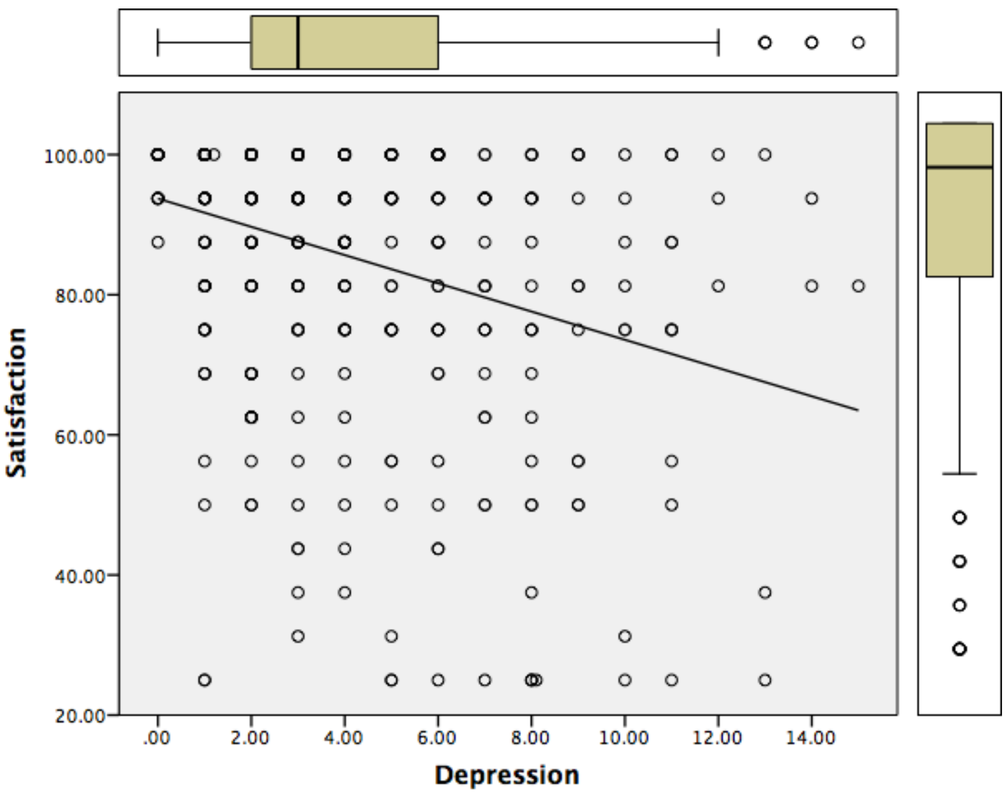


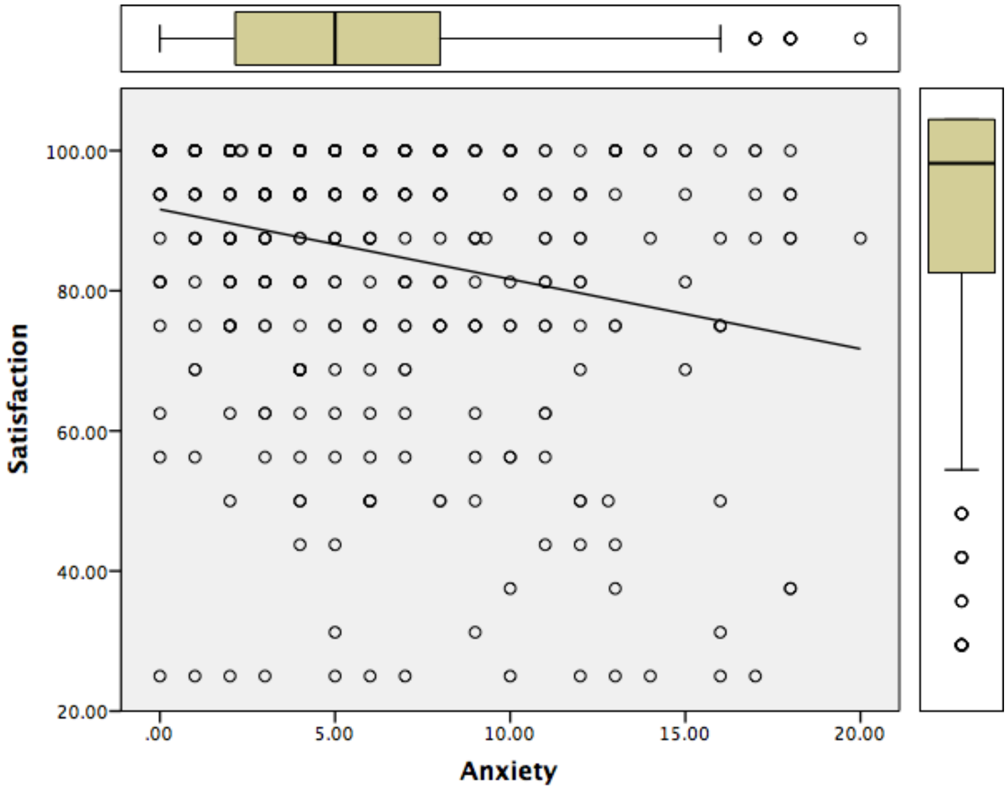
100.00
80.00
60.00
40.00
20.00
Satisfaction
5.00
10.00
15.00
20.00
25.00
Internality



100.00
80.00
60.00
40.00
20.00
Satisfaction
.00
10.00
20.00
30.00
40.00
50.00
60.00
PCS

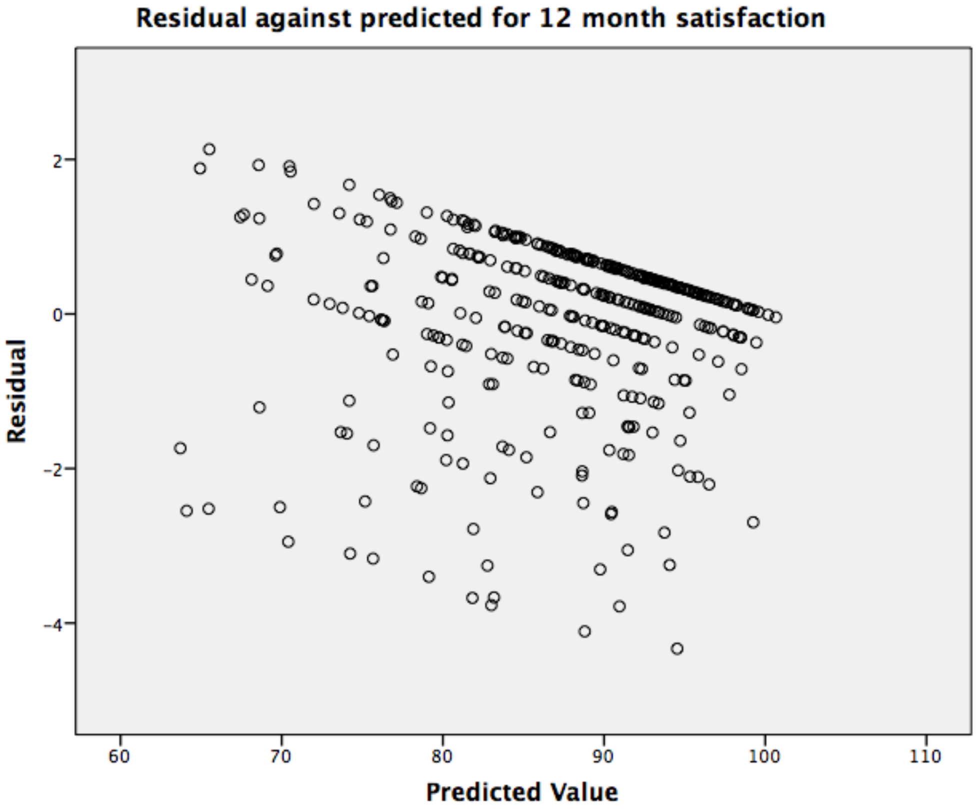

100.00
80.00
60.00
40.00
20.00
Satisfaction
20.00
40.00
60.00
80.00
MCS


100.00
80.00
60.00
40.00
20.00
Satisfaction
.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00
Depression



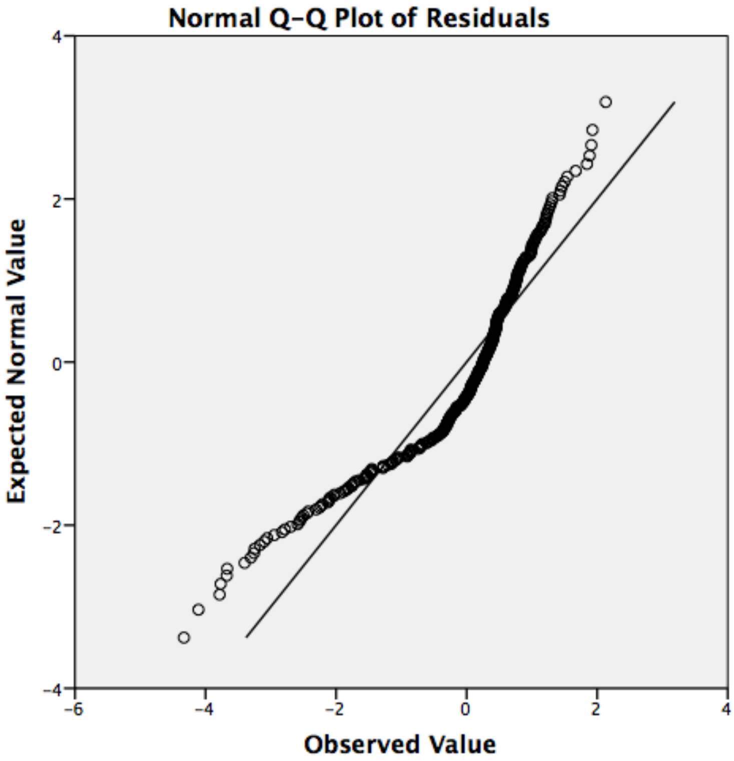
Homoscedasticity

This was tested using a residual versus prediction scatterplot. An even spread of residual values across the range of predicted values suggests heteroscedasticity and linearity.

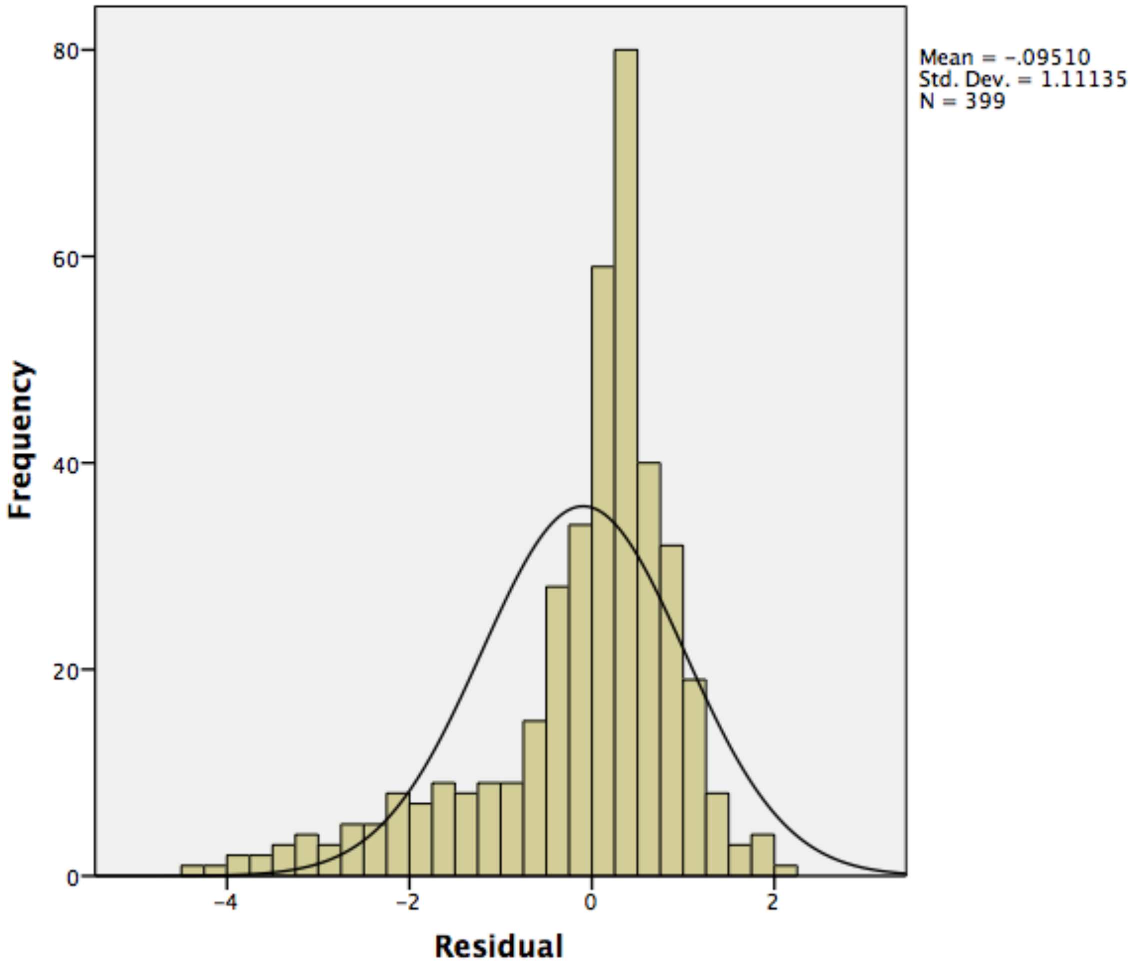


Normality of residuals

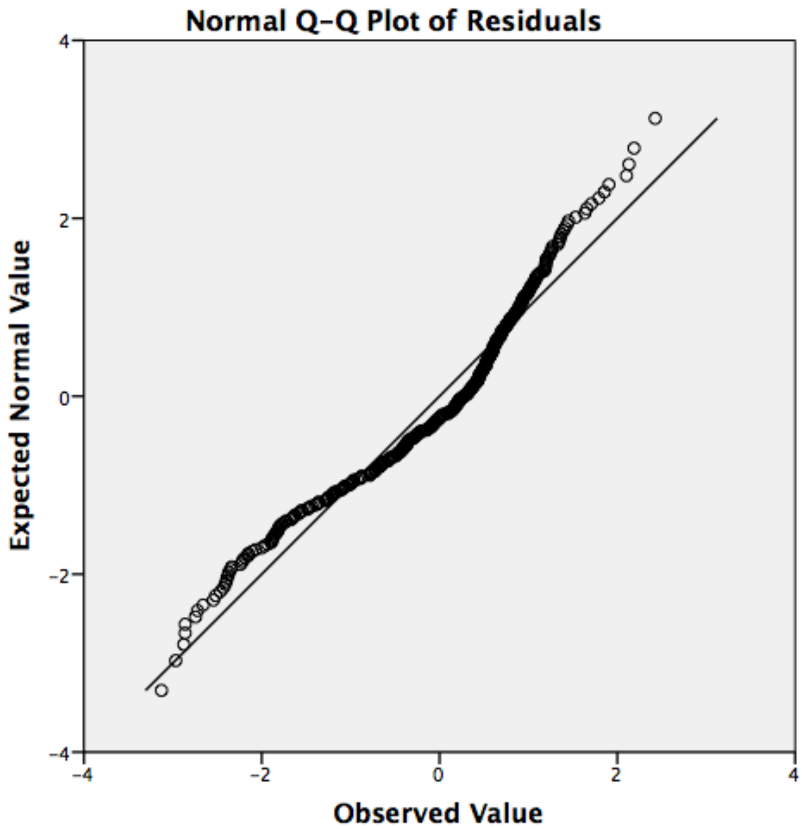
The QQ plot below demonstrates that the residuals were not normally distributed.



The plot suggested the data was left skewed (as demonstrated by the histogram in below.



A common transformation to deal with left skewed data is to square the data (Tukey's ladder of transformations).[165] Therefore, the response variable was squared and cubed, and models compared. The cubed model provided the following QQ plot:



These data still display some skewness, but I felt that the requirement for linear regression was met.

Decision regret

To assess for linearity between explanatory variables and the logit of the response variable the Box-Tidwell procedure was used. This models interaction between the explanatory variable and its natural log. Any statistically significant results (with a Bonferroni correction) suggest non-linearity. The table is available on the next page.

	B	S.E.	Wald	Sig.	Exp(B)	95% CI Lower Bound	95% CI Upper Bound
Age	-1.066	2.775	0.147	0.701	0.345	0.001	79.259
Gender (1)	-14.206	8.435	2.837	0.092	0	0	10.235
Baseline OKS	-0.759	0.822	0.853	0.356	0.468	0.094	2.344
BMI	0.383	1.624	0.056	0.814	1.466	0.061	35.39
Severe Arthritis	-0.642	0.725	0.785	0.375	0.526	0.127	2.178
Joint Count	-2.059	0.781	6.955	0.008	0.128	0.028	0.589
Back Pain	-0.485	0.748	0.421	0.517	0.616	0.142	2.666
Comorbidities	1.401	1.815	0.596	0.44	4.06	0.116	142.494
Live Alone	0.061	0.766	0.006	0.937	1.063	0.237	4.766
Deprivation Score	0.223	0.288	0.598	0.44	1.25	0.71	2.2
Previous Arthroscopy	-0.138	0.647	0.046	0.831	0.871	0.245	3.097
Expectations	-0.412	2.973	0.019	0.89	0.662	0.002	224.558
Helplessness	-2.031	2.932	0.48	0.488	0.131	0	41.087
Internality	4.691	5.4	0.754	0.385	108.922	0.003	430534 2.661
PCS	1.119	1.15	0.947	0.331	3.062	0.321	29.169
MCS	-0.274	0.911	0.091	0.763	0.76	0.127	4.534
Depression	0.905	1.552	0.34	0.56	2.472	0.118	51.775
Anxiety	-0.229	0.68	0.113	0.737	0.796	0.21	3.019
Age by Baseline OKS	0.009	0.006	2.119	0.145	1.009	0.997	1.022
Age by Gender(1)	0.169	0.098	2.981	0.084	1.184	0.977	1.433
Age by MCS	-0.004	0.004	0.871	0.351	0.996	0.988	1.004
Age by Depression	-0.008	0.017	0.206	0.65	0.992	0.96	1.026
Gender(1) by O Baseline OKS	0.01	0.1	0.009	0.923	1.01	0.83	1.228
Gender(1) by MCS	0.03	0.071	0.176	0.675	1.03	0.896	1.185
Depression by Gender(1)	0.32	0.289	1.226	0.268	1.377	0.781	2.427
MCS by Baseline OKS	-0.001	0.006	0.035	0.851	0.999	0.988	1.01
Age by LnAge	0.211	0.529	0.16	0.689	1.236	0.438	3.482
LnOKS by Baseline OKS	0.042	0.227	0.034	0.854	1.043	0.669	1.626
BMI by LnBMI	-0.077	0.359	0.046	0.83	0.926	0.458	1.871
Joint Count by LnJoint Count	0.67	0.265	6.385	0.012	1.954	1.162	3.285
Comorbidities by LnComorbidities	-0.58	0.782	0.549	0.459	0.56	0.121	2.594
Deprivation Score by LnDeprivation	-0.055	0.069	0.638	0.424	0.946	0.826	1.084
Expectations by LnExpectations	0.092	0.639	0.021	0.886	1.096	0.313	3.834
Helplessness by LnHelplessness	0.547	0.834	0.431	0.512	1.728	0.337	8.857
Internality by LnInternality	-1.21	1.452	0.694	0.405	0.298	0.017	5.139
LnPCS by PCS	-0.277	0.286	0.942	0.332	0.758	0.433	1.327
LnMCS by MCS	0.102	0.203	0.254	0.615	1.108	0.744	1.648
Depression by LnDepression	-0.16	0.309	0.267	0.605	0.853	0.466	1.561
Anxiety by LnAnxiety	0.1	0.221	0.204	0.651	1.105	0.717	1.703
Constant	-1.251	52.624	0.001	0.981	0.286		

9.7 Appendix VII: The effect of expectation on satisfaction in total knee replacements: a systematic review.

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DOI 10.1186/s40064-016-1804-6

SpringerPlus
a SpringerOpen Journal

REVIEW

Open Access

The effect of expectation on satisfaction in total knee replacements: a systematic review

Timothy Barlow, Tamsyn Clark, Mark Dunbar, Andrew Metcalfe and Damian Griffin*

Abstract

Total knee replacement has reliably been shown to have a beneficial effect in knee osteoarthritis; however, around 17 % of patients are dissatisfied with the result. A commonly proposed mechanism driving the dissatisfaction rate is a discrepancy between expected and actual/perceived outcome. Our aim was to conduct a systematic review examining any association between pre-operative expectations and satisfaction. A comprehensive electronic search strategy was used to identify studies from MEDLINE, EMBASE, and the Cochrane Library from inception until May 2015. Data was extracted according to PRISMA guidelines and an online, published protocol. Four studies are included in this review. One study found an association between expectations and satisfaction. Different measures of expectation and satisfaction were used in all studies. To date, there is no consensus on how expectations or satisfaction should be measured, and a large number of studies that have the available information failed to conduct the relevant sub-group analysis. Further elucidation and consensus of how to measure expectations and satisfaction around joint replacement would aid this area of study greatly. On the basis of the current evidence it appears expectations have a small effect, if any, on satisfaction after knee replacement.

Keywords: Satisfaction, Expectation, Knee replacement

Background

Primary osteoarthritis (OA) of the knee is a condition that can lead to loss of knee function, pain, and deterioration in quality of life. This in turn can lead to difficulty working, performing activities of daily living, stress, and depression (Smith and Zautra 2008). Ten percent of the U.K. population over the age of 55 suffers from pain as a result of knee osteoarthritis (Peat et al. 2006). With an ageing population this condition will present more and more of a health burden.

Total knee replacement has reliably been shown to have a beneficial effect (Juni et al. 2006), and over 90,000 knee replacements were performed in England and Wales in 2014, with over 90 % of these for OA (Registry 2014). However a sub group of patients exist that have poorer outcomes following knee replacement. Some studies show dissatisfaction rates as high as 17 % (Hawker et al. 2009).

The question of what factors drive this high rate of dissatisfaction is one that has received much attention in the literature. Most previous work has focused on the effect of different prostheses and surgical factors on outcome and this has only been able to account for a small proportion of the variability in outcome (Callahan et al. 1994; Judge et al. 2012). There is growing evidence that factors intrinsic to the patient may significantly affect outcome (Santaguida et al. 2008). Such factors include psychological factors, demographics, and patient expectations (Heck et al. 1998; Lingard et al. 2004; Mannion et al. 2009).

Investigations into expectations are complex, as different authors describe different constructs under the term expectation (Haanstra et al. 2012). For the purposes of this paper, we describe expectations as "cognitions regarding probable future events" (Haanstra et al. 2012). This specifically excludes self efficacy, which can be defined as "beliefs in one's capabilities to organize and execute the courses of action required to produce given attainments" (Bandura 1977). A further clarification

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needs to be made between expectations and expectation fulfilment. Pre-operatively a patient has expectations (a series of beliefs about the outcome of the operation), post-operatively a patient can decide if those expectations have been met or not (expectation fulfilment) (Scott et al. 2012). Using these definitions, it is logical that patients whose expectations are not fulfilled are likely to be less satisfied. This has been demonstrated in the literature (Scott et al. 2012), but a further layer of complexity exists when we consider the shift in patients' view of what is healthy or to be expected over the course of their treatment (response shift) (Razmjou et al. 2006). Even with this response shift, expectation fulfilment is linked to outcome after knee replacements (Scott et al. 2012; Clement et al. 2014).

However, what remains unclear is the relationship between pre-operative expectations and satisfaction. Indeed, the potential for altering satisfaction based on appropriate management of pre-operative expectations may be a worthwhile approach to tackling the issue of high dissatisfaction rates. It will also provide clinicians with information on how critical managing expectations are when satisfaction is the endpoint of interest. While previous attempts at synthesising the evidence exist (Haanstra et al. 2012; Dyck et al. 2014; Waljee et al. 2014), none have set out to answer this basic and fundamental question. Specifically, most reviews have not had satisfaction as the outcome of interest, and included both knee and hip replacements together (Haanstra et al. 2012; Dyck et al. 2014; Waljee et al. 2014). These operations differ not only by outcome (and, one would expect, by pre-operative expectation) (Registry 2014), but also by patient demographics and potentially aetiology (Grotle et al. 2008; Jokela et al. 2013). Therefore, when examining expectations, combining these operations is potentially flawed.

The aim of this systematic review is to determine if pre-operative expectations affect post-operative satisfaction in knee replacements.

Patients and methods

In line with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (PRISMA 2012) the protocol was submitted to the PROSPERO database prior to the performance of the systematic review. The reference number is CRD42015023216 and is available at http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015023216.

Search strategy

A comprehensive electronic search strategy was used to identify studies from MEDLINE (Medical Literature Analysis and Retrieval System Online, Bethesda, Maryland, USA), EMBASE (Excerpta Medical Database, Amsterdam, The Netherlands) and the Cochrane Library using all available data from their inception until May 2015.

The search strategy is available in the supplementary materials and was designed to be as comprehensive as possible in order to mitigate the risk of producing 'precise but spurious results' (Egger et al. 1998) (Additional file 1).

Eligibility criteria

Studies were eligible for inclusion if they were prospective studies observing the effect of expectation on satisfaction in knee replacement for osteoarthritis. Studies where information was retrieved from a database were also included if the pre-operative expectation was collected prospectively. Case series and case–control studies were not included as there is a significant potential for selection bias with these types of study design (Sara et al. 2009). Only studies that were presented in English were included in the analysis.

The subjects included in each study were patients about to undergo total knee replacement with a diagnosis of osteoarthritis. Where patients with other arthritic diseases (e.g. traumatic arthritis, inflammatory arthritis), or patients who had undergone revision knee replacement, made up more than 5 % of the study population the studies were excluded. However, studies containing mixed groups of patients were included if there was subgroup analysis that clearly differentiated the population of interest. Studies that included both hip and knee replacement patients were only included where there was a subgroup analysis of the knee patients. Authors of papers that had both hip and knee replacement patients, but where no subgroup analysis was presented, were contacted and asked if any subgroup analysis was done, and to forward it on if it had been.

Any study that collected information on patient expectations retrospectively was excluded as this has been shown to be unreliable (Razmjou et al. 2006).

Expectation and satisfaction measurements

Many tools exist for the measurement of expectation and satisfaction. No paper was excluded on the basis of its measurement method, although these are commented on.

Analytic methods

Studies had to have made some attempt to associate satisfaction with expectation. Various methods of regression or correlation analysis were acceptable as long as they were clearly explained in the methods section in order to determine that their use was appropriate for the type of data collected.

Quality assessment

The Newcastle Ottawa Scale provides a system for assessing quality across three domains: selection, comparability, and outcome (Stang 2010). Each domain is scored with a star rating system. A summary score is not provided in an attempt to provide data on the biases inherent in the study design.

Data extraction

After the initial search was performed the studies were screened for eligibility in sequential rounds where their relevance was assessed using at first their titles and abstracts, and finally full review of the paper. Two reviewers (TC and TB), who were both experienced in performing systematic reviews, then independently re-examined each full paper to ensure that they met the inclusion criteria. Relevant data was extracted and a quality assessment performed independently by both reviewers, resolving any differences through discussion and review.

Due to the nature and heterogeneity of the analyses used in the studies, combined with the heterogeneity of the measurements of expectations and satisfaction, no formal meta-analysis was performed.

Results

Description of studies

Our search returned 762 studies. Of these some were duplicates from multiple databases that due to a technical limitation had to be removed by hand during the title search. Figure 1 is a flow chart detailing the studies that were excluded. We have included four studies in this review (Table 1).

Quality assessment

Table 2 describes the quality assessment using the Newcastle Ottawa scale. All studies were judged to be of similar quality.

Expectations and satisfaction

Of the four studies included in the review the sample size varied from 44 to 598. A different method of measuring expectations was used in each study, and a different method for measuring satisfaction was used in each study (please see Additional File 2 for description of measures used). One study was international in nature and was also the largest by almost double the sample size (Lingard et al. 2006). All other studies were single centre (Kiran et al. 2015; Vissers et al. 2010; Mannion et al. 2009).

Three studies conducted a univariate analysis (Kiran et al. 2015; Vissers et al. 2010), with only one study finding an association between pain and function expectations and satisfaction (Mannion et al. 2009).

Two studies conducted a multivariate analysis and neither found a significant association between expectations and satisfaction (Lingard et al. 2006; Mannion et al. 2009). One study had the largest sample size and did not conduct univariate analysis (Lingard et al. 2006). The second study, that had found an association in the univariate model, did not find an association in the multivariate model; however, they had a sample size of 87, with over 5 covariates in the model, and had included expectation fulfilment in the multivariate model (Mannion et al. 2009). It is therefore questionable if this study had the necessary power to conduct this analysis, and the logic of including expectation fulfilment (which would be expected to account for the same variation in the final model as pre-operative expectation) is questionable.

Two studies reported positive finding of expectation related to other outcome measures. Kiran found that pre-operative expectation of no pain gave higher (better) OKS score ($p < 0.01$) (Kiran et al. 2015), and Lingard found that pre-operative expectation of no pain resulted in better WOMAC pain scores ($p = 0.039$) and pre-operative expectation of not needing a walking aid resulted in better WOMAC function score ($p < 0.0001$) (Lingard et al. 2006).

Discussion

Overall, one study out of four found an association between expectation and satisfaction. This could be due to: each study measuring slightly different constructs of "expectation" and "satisfaction"; the effect of expectation on satisfaction may be small, and of dubious clinical relevance.

This study has highlighted several issues surrounding expectation and satisfaction in knee replacements. The first key finding is the multiple measures used by each study to evaluate expectation and satisfaction. There is a great deal of difficulty in measuring these constructs, and multiple theoretical models exist to try and explain some of the complexity. For example the latent state-trait theory suggests that with measurement instruments we measure a persons state, which will depend upon the person (the person's traits), the situation, and the interaction between the person and situation (Steyer et al. 1999). This highlights the difficulty in measuring these constructs consistently and accurately, and may go some way to explain the low numbers of studies examining this key issue. It seems likely that until the orthopaedic community can reach a consensus on what is important to measure, and how to measure it, progress will be slow.

The second key issue is the low number of studies that have examined this issue within the literature. Many studies have examined expectation fulfilment (Scott et al. 2012; Clement et al. 2014; Kumar et al. 2015; Adie et al. 2012), and there were multiple studies that measured pre-operative expectation and satisfaction but were

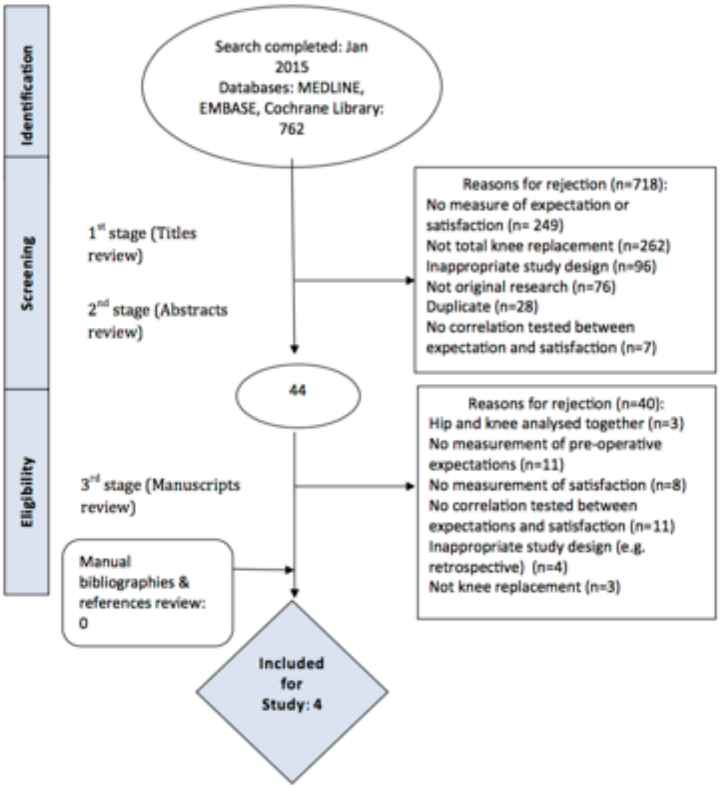

Fig. 1 Flow chart of included studies

excluded from this review because they did not make any attempt to test for an association (Suda et al. 2010; Clement et al. 2014; Kumar et al. 2015), or they included hips and knees as one cohort (Gonzalez Saenz de Tejada et al. 2014; Brokelman et al. 2008; Gandhi et al. 2009). This is a key finding is itself, as pre-operative expectations would be an ideal target for modification if an association were present. It may be that the difficulty surrounding reliable measurements of these constructs is responsible.

Limitations of this review include the lack of formal meta-analysis, which was not possible due to the heterogeneity within the papers included. English language articles were specified in the inclusion criteria for full paper review, but not in the search strategy. Therefore, although the possibility of missing important information from other sources existed, in practice there were no fully published papers in other languages that would have met the inclusion criteria.

There was some variation in the length of follow up between studies. This has the potential to introduce a form of timing bias as it has been shown that the functional status of knees after replacement can improve for around 2 years following surgery (Pynsent et al. 2005). Studies that did not show associations in some domains might well have done so if the length of follow up was extended.

Table 1 Included studies

Author	Year	Title	Study design	Sample size	Time to follow up	Measure of expectation	Measure of satisfaction	Analysis	Link between expectation and satisfaction
Kiran et al.	2015	Variations in good patient reported outcomes after total knee arthroplasty	Cohort	365	2 years	Two questions on a 3 and 4 part Likert scale	Global satisfaction (yes/no)	Univariate	No
Lingard et al.	2006	Patient expectations regarding total knee arthroplasty: differences among the United States, United Kingdom, and Australia	Cohort	598	1 year	Four questions on a 4 part likert scale	Four questions using a four part likert scale	Multivariate	No
Mannion et al.	2009	The role of patient expectations in predicting outcome after total knee arthroplasty	Cohort	87	2 years	Three questions with free text and likert scale	Global satisfaction four part likert	Univariate and multivariate	Univariate model—yes Multivariate model—no
Vissers et al.	2010	Functional capacity and actual daily activity do not contribute to patient satisfaction after total knee arthroplasty	Cohort	44	6 months	Three questions on a four part likert scale	Global satisfaction five part likert scale	Univariate	No

Table 2 Quality assessment

Study	Selection	Comparability	Outcome
Kiran et al. (2015)	4	0	1
Vissers et al. (2010)	4	0	2
Mannion et al. (2009)	4	1	1
Lingard et al. (2006)	4	1	2

Systematic reviews are always subject to publication bias and in particular the delay or lack of publication of studies with negative findings (Stern and Simes 1997). We have tried to minimise this by including all archived, published research from each of our searched databases, but the possibility remains that some evidence may remain unpublished. This is more likely from older, less well-designed studies, as the resources required performing a high quality modern, observational study would dictate publication irrespective of the findings. As the concepts and subsequent measurement of expectations and satisfaction are relatively new, it is likely we have included all relevant studies.

Some other studies have been conducted examining the association between expectation in hip and knee and satisfaction. Of these, a study conducted by Gonzalez et al. that was multicentre and included a multivariate analysis demonstrated a significant effect of expectations on satisfaction (Gonzalez Saenz de Tejada et al. 2014), whereas two others, with smaller sample sizes and from single centres, did not (Brokelman et al. 2008; Gandhi et al. 2009). This does tend to suggest that the construct of expectation and satisfaction that is being measured is key and can alter the significance of the result.

A further issue surrounds that of the clinical significance of our result. Certainly, with regard to satisfaction, managing a patient's pre-operative expectation appears to have little effect on post-operative satisfaction. However, this is not the whole picture, as outcome can be measured in a multitude of different ways. Patient Reported Outcome Measures (PROMs) show associations with pre-operative expectations in multiple studies (Kiran et al. 2015; Lingard et al. 2006; Mahomed et al. 2002), and expectations are associated with length of stay and discharge destination (Halawi et al. 2015a, b).

Conclusion

One out of four studies found evidence of an association between pre-operative expectations and satisfaction. While this could be interpreted as either no effect, or a small, clinically insignificant effect, we would caution against a move to abandon management of patient expectations for two reasons: expectations and satisfaction are difficult constructs to measure, and the papers included here may be measuring different aspects of these constructs; satisfaction is not the only outcome measure available, and other outcome measures are related to pre-operative expectations. One of the major findings of this paper is the lack of large, high quality, studies that have examined this key issue, and the lack of consensus within the literature on how to measure expectation and satisfaction.

Additional files

Additional file 1. Search strategy.
Additional file 2. Measures of expectation and satisfaction.

Authors' contributions
TB conceived, designed, conducted the search, extracted data, and wrote the paper. TC extracted data and helped draft the paper. MD designed and helped draft the paper. DG designed and helped draft the paper. All authors read and approved the final manuscript.

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Competing interests
TB received salary from Arthritis Research U.K. while performing this review. DG and TB have received project grant funding from Arthritis Research U.K. The authors declare that they have no competing interests.

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References

Adie S, Dao A, Harris IA, Naylor JM, Mittal R (2012) Satisfaction with joint replacement in public versus private hospitals: a cohort study. ANZ J Surg 82(9):616–624
Bandura A (1977) Self-efficacy: toward a unifying theory of behavioral change. Psychol Rev 84(2):191–215
Brokelman R, van Loon C, van Susante J, van Kampen A, Veth R (2008) Patients are more satisfied than they expected after joint arthroplasty. Acta Orthop Belg 74(1):59–63
Callahan CM, Drake BG, Heck DA, Dittus RS (1994) Patient outcomes following tricompartmental total knee replacement. A meta-analysis. JAMA 271(17):1349–1357
Clement ND, Macdonald D, Patton JT, Burnett R (2014) Post-operative Oxford knee score can be used to indicate whether patient expectations have been achieved after primary total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. doi:10.1007/s00167-014-2865-0
Dyck BA, Zywiel MG, Mahomed A, Gandhi R, Perruccio AV, Mahomed NN (2014) Associations between patient expectations of joint arthroplasty surgery and pre- and post-operative clinical status. Expert Rev Med Devices 11(4):403–415. doi:10.1586/17434440.2014.916208
Egger M, Schneider M, Davey Smith G (1998) Spurious precision? Meta-analysis of observational studies. BMJ 316(7125):140–144
Gandhi R, Davey JR, Mahomed N (2009) Patient Expectations predict greater pain relief with joint arthroplasty. J Arthroplasty 24(5):716–721. doi:10.1016/j.arth.2008.05.016
Gonzalez Saenz de Tejada M, Escobar A, Bilbao A, Herrera-Espineira C, Garcia-Perez L, Aizpuru F, Sarasqueta C (2014) A prospective study of the association of patient expectations with changes in health-related quality of life outcomes, following total joint replacement. BMC Musculoskelet Disord 15:248. doi:10.1186/1471-2474-15-248

Grotle M, Hagen KB, Natvig B, Dahl FA, Kvien TK (2008) Obesity and osteoarthritis in knee, hip and/or hand: an epidemiological study in the general population with 10 years follow-up. BMC Musculoskelet Disord 9:132. doi:10.1186/1471-2474-9-132

Haanstra TM, Van Den Berg T, Ostelo RW, Poolman RW, Jansma IP, Cuijpers P, de Vet HCW (2012) Systematic review: do patient expectations influence treatment outcomes in total knee and total hip arthroplasty? Health Qual Life Outcomes. doi:10.1186/1477-7525-10-152

Halawi MJ, Vovos TJ, Green CL, Wellman SS, Attarian DE, Bolognesi MP (2015a) Patient expectation is the most important predictor of discharge destination after primary total joint arthroplasty. J Arthroplasty 30(4):539–542. doi:10.1016/j.arth.2014.10.031

Halawi MJ, Vovos TJ, Green CL, Wellman SS, Attarian DE, Bolognesi MP (2015b) Preoperative predictors of extended hospital length of stay following total knee arthroplasty. J Arthroplasty 30(3):361–364. doi:10.1016/j.arth.2014.10.025

Hawker GA, Badley EM, Croxford R, Coyte PC, Glazier RH, Guan J, Harvey BJ, Williams JI, Wright JG (2009) A population-based nested case–control study of the costs of hip and knee replacement surgery. Med Care 47(7):732–741. doi:10.1097/MLR.0b013e3181934553

Heck DA, Robinson RL, Partridge CM, Lubitz RM, Freund DA (1998) Patient outcomes after knee replacement. Clin Orthop Relat Res 356:93–110

Jokela M, Hintsanen M, Hakulinen C, Batty GD, Nabi H, Singh-Manoux A, Kivimaki M (2013) Association of personality with the development and persistence of obesity: a meta-analysis based on individual-participant data. Obes Rev 14(4):315–323. doi:10.1111/obr.12007

Judge A, Arden NK, Cooper C, Kassim Javaid M, Carr AJ, Field RE, Dieppe PA (2012) Predictors of outcomes of total knee replacement surgery. Rheumatology (Oxford) 51(10):1804–1813. doi:10.1093/rheumatology/kes075

Juni P, Reichenbach S, Dieppe P (2006) Osteoarthritis: rational approach to treating the individual. Best Pract Res Clin Rheumatol 20(4):721–740. doi:10.1016/j.berh.2006.05.002

Kiran A, Bottomley N, Biant LC, Javaid MK, Carr AJ, Cooper C, Field RE, Murray DW, Price A, Beard DJ, Arden NK (2015) Variations in good patient reported outcomes after total knee arthroplasty. J Arthroplasty. doi:10.1016/j.arth.2015.02.039

Kumar M, Battepathi P, Bangalore P (2015) Expectation fulfilment and satisfaction in total knee arthroplasty patients using the 'PROFEX' questionnaire. Orthop Traumatol Surg Res. doi:10.1016/j.otsr.2014.12.016

Lingard EA, Katz JN, Wright EA, Sledge CB (2004) Predicting the outcome of total knee arthroplasty. J Bone Joint Surg Am 86-A(10):2179–2186

Lingard EA, Sledge CB, Learmonth ID (2006) Patient expectations regarding total knee arthroplasty: differences among the United States, United Kingdom, and Australia. J Bone Joint Surg Am 88(6):1201–1207. doi:10.2106/jbjs.e.00147

Mahomed NN, Liang MH, Cook EF, Daltroy LH, Fortin PR, Fossel AH, Katz JN (2002) The importance of patient expectations in predicting functional outcomes after total joint arthroplasty. J Rheumatol 29(6):1273–1279

Mannion AF, Kampfen S, Munzinger U, Kramers-de Quervain I (2009) The role of patient expectations in predicting outcome after total knee arthroplasty. Arthritis Res Ther 11(5):R139. doi:10.1186/ar2811

Peat G, Thomas E, Duncan R, Wood L, Hay E, Croft P (2006) Clinical classification criteria for knee osteoarthritis: performance in the general population and primary care. Ann Rheum Dis 65(10):1363–1367. doi:10.1136/ard.2006.051482

PRISMA (2012) Preferred reporting items for systematic reviews and meta-analyses. PRISMA. Accessed Feb 2012

Pynsent PB, Adams DJ, Disney SP (2005) The Oxford hip and knee outcome questionnaires for arthroplasty. J Bone Joint Surg Br 87(2):241–248

Razmjou H, Yee A, Ford M, Finkelstein JA (2006) Response shift in outcome assessment in patients undergoing total knee arthroplasty. J Bone Joint Surg 88(12):2590–2595. doi:10.2106/JBJS.F.00283

Registry NJ (2014) National Joint Registry. Accessed Jan 2015

Santaguida PL, Hawker GA, Hudak PL, Glazier R, Mahomed NN, Kreder HJ, Coyte PC, Wright JG (2008) Patient characteristics affecting the prognosis of total hip and knee joint arthroplasty: a systematic review. Can J Surg 51(6):428–436

Sara G, Nicky B, Mireille T, Paul E, Sylvia R (2009) Uncovering selection bias in case-control studies using Bayesian poststrati ctation. Biostatistics 10(1):17–31

Scott CE, Bugler KE, Clement ND, MacDonald D, Howie CR, Biant LC (2012) Patient expectations of arthroplasty of the hip and knee. J Bone Joint Surg Br 94(7):974–981. doi:10.1302/0301-620x.94b7.28219

Smith BW, Zautra AJ (2008) The effects of anxiety and depression on weekly pain in women with arthritis. Pain 138(2):354–361. doi:10.1016/j.pain.2008.01.008

Stang A (2010) Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol 25(9):603–605. doi:10.1007/s10654-010-9491-z

Stern JM, Simes RJ (1997) Publication bias: evidence of delayed publication in a cohort study of clinical research projects. BMJ 315(7109):640–645

Steyer R, Schmitt M, Eid M (1999) Latent state-trait theory and research in personality and individual differences. Eur J Pers 13(13):389–408

Suda AJ, Seeger JB, Bitsch RG, Krueger M, Clarius M (2010) Are patients' expectations of hip and knee arthroplasty fulfilled? A prospective study of 130 patients. Orthopedics. doi:10.3928/01477447-20100104-7

Vissers MM, de Groot IB, Reijman M, Bussmann JB, Stam HJ, Verhaar JA (2010) Functional capacity and actual daily activity do not contribute to patient satisfaction after total knee arthroplasty. BMC Musculoskelet Disord 11:121. doi:10.1186/1471-2474-11-121

Waljee J, McGlinn EP, Sears ED, Chung KC (2014) Patient expectations and patient-reported outcomes in surgery: a systematic review. Surgery 155(5):799–808. doi:10.1016/j.surg.2013.12.015

9.8 Appendix VIII: Patients' decision-making in total knee arthroplasty. A systematic review of qualitative research.

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Patients' decision making in total knee arthroplasty

A SYSTEMATIC REVIEW OF QUALITATIVE RESEARCH

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Objectives
A patient-centred approach, usually achieved through shared decision making, has the potential to help improve decision making around knee arthroplasty surgery. However, such an approach requires an understanding of the factors involved in patient decision making. This review's objective is to systematically examine the qualitative literature surrounding patients' decision making in knee arthroplasty.

Methods
A systematic literature review using Medline and Embase was conducted to identify qualitative studies that examined patients' decision making around knee arthroplasty. An aggregated account of what is known about patients' decision making in knee arthroplasties is provided.

Results
Seven studies with 234 participants in interviews or focus groups are included. Ten themes are replicated across studies, namely: expectations of surgery; coping mechanisms; relationship with clinician; fear; pain; function; psychological implications; social network; previous experience of surgery; and conflict in opinions.

Conclusions
This review is helpful in not only directing future research to areas that are not understood, or require confirmation, but also in highlighting areas that future interventions could address. These include those aimed at delivering information, which are likely to affect the satisfaction rate, demand, and use of knee arthroplasties.

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Keywords: Decision making, arthroplasty, knee

Article focus
- Patients' decision making plays a central role in preference-based health decisions.
- This article's aim is to provide an aggregated account of the factors that influence patients' decision making when considering total knee arthroplasty.

Key messages
- We identified ten themes that were replicated across studies.
- The themes interact with each other.
- The themes have varying influences across different patients and different healthcare settings.

Strengths and limitations
- Robust and reproducible search criteria were used, accepting the limitations of electronic indexing of qualitative work.
- No synthesis of included studies was conducted. This is a controversial topic, and currently no consensus exists as to the value, or the methods, in qualitative synthesis.
- All included papers only examined patients at one stage in the process of care. The stage of decision making is likely to be an important element in understanding the decision making process.

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Introduction

Understanding patients' decision making has particular relevance during patients' deliberation over having a knee arthroplasty. It has the potential to improve the information given to patients, patient-centred care, and to inform patient decision aids. Improved pre-operative counselling could help address three problematic areas facing knee arthroplasty services: a high dissatisfaction rate; increasing demand with financial constraints; and a variation in the use of knee arthroplasties.

The rate of dissatisfaction after knee arthroplasty surgery is around 17%, although estimates vary.[1] One of the potential factors implicated in the high dissatisfaction rate is patient expectations.[2] Patients with unrealistically high expectations may drive a high dissatisfaction rate.[2] Understanding how expectations of outcome affect the decision making process may help in understanding the dissatisfaction rate, and may even aid methods to decrease it (particularly interventions aimed at providing information).

There is increasing demand for knee arthroplasties combined with increasing financial pressure.[3,4] This is not specific to knee arthroplasties, but if current trends in the use of total knee arthroplasty (TKA) hold true, we are likely to see at least a three-fold increase in demand by 2035.[5] Interventions to improve patient-centred care through shared decision making (which requires an understanding of patient decision making) have demonstrated a decrease in the uptake of preference-based elective operations, but no studies have been conducted in knee arthroplasty surgery.[6,7]

There is a significant amount of variation in the use of knee arthroplasties. Differences in expenditure of almost four fold are demonstrated between Primary Care Trusts with regard to inpatient knee arthroplasty costs - those trusts with the highest expenditure treat patients with the best pre-operative patient-reported outcome measures (PROMs) scores.[8] Some of this variation is warranted in that it reflects patient preference: Hawker et al[9] report that in some groups of patients only one third that would fulfil a needs assessment would be willing to undergo a joint arthroplasty. However, it is clear that not all the variation is warranted (i.e. due to patient need or preference). For example, orthopaedic surgeons and general practitioners have been reported to be less likely to refer a woman with osteoarthritis (OA) of the knee for knee arthroplasty than they would a man.[10] Therefore, the variation observed in utilisation rates is likely to be due in part to patient preference, and an understanding of how patients make decisions about having a TKA should explain some of this variation.

Various attempts at identifying how patients make decisions about knee surgery, and what factors are important to them, have been conducted. Interestingly, many studies have examined both hip and knee patients as one cohort. Additionally, historic attempts at synthesising the qualitative literature on this topic have likewise included both hip and knee patients as one patient group.[11] Although there are clear similarities between these groups, there are significant differences that make combining these populations potentially unsound.

Firstly, there is the significant difference in the 'success' rate of hip and knee arthroplasties. TKAs have a dissatisfaction rate of around 17%.[1,12] Hip arthroplasties have significantly better outcomes regarding satisfaction, pain, and function.[13] Ibrahim et al[14] examined the influence of expectations as an explanatory factor in some of the variation in utilisation rates of joint arthroplasty, and found that it explains some of the variation. Therefore, knee arthroplasty decision making is likely to be different to that for hip arthroplasties, as the outcome is not the same.

Secondly, the population that develop hip arthritis are different to the population that develop knee arthritis. A recent study including almost 2000 participants found that body mass index (BMI) was correlated with the development and progression of OA of the knee, but not hip OA.[15] This is particularly relevant to decision making, as people with higher BMIs display different psychological profiles to the general population.[16]

Therefore, people who develop hip and knee OA are likely to be different populations, with different psychological profiles. Additionally, the outcome, and therefore expectation, of the operations are different.

An understanding of patients' decision making will be helpful in not only enabling high quality, patient-centred interactions, but in highlighting areas that future interventions could address (particularly interventions aimed at delivering information).

This review aggregates the qualitative literature surrounding patients' decision making in knee arthroplasty surgery. The aim of this review was to provide an aggregation of studies (c.f. a synthesis of qualitative studies) – the difference, as Sandelowski, Barroso and Voils[17] describe, is accumulation and summary, rather than transformation. This represents an approach consistent with a "lines argument synthesis", defined as "building up a picture of the whole" and represents what Pantoja described as a realist synthesis with narrative review,[18] however, the term synthesis here refers to the combination of results, rather than any second or third order interpretation of them.

Materials and Methods

We conducted a literature search of Medline and Embase in January 2015. Subject and topic terms (Knee, Knee prosthesis, Knee replacement, Knee arthroplasty and Decision making) were included, both as free text and indexed headings. A bibliographic search of all studies retrieved for full text analysis (whether included in the final review or not) was conducted. This search strategy is consistent with that used by the Evidence for Policy and Practice Information Centre.[19]

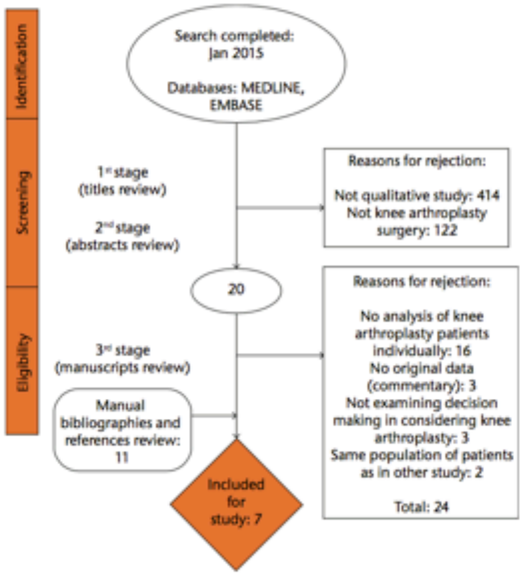

Fig. 1

Flow diagram of included studies

Studies that reported qualitative data on the decision making process in knee arthroplasties were included. The lead author selected the relevant papers, and conducted a bibliographic search. All full text papers retrieved were screened by a second author (DB) to provide consensus that papers were reporting qualitative findings on decision making. We did not specifically exclude survey data, however, such papers were required to provide insights into decision making over and above reporting descriptive or inferential statistics. The eligibility criteria were:

Inclusion - Findings on how and why patients make decisions regarding knee arthroplasty.

- Recognised as qualitative research.

Exclusion - Knee patients' decision making not reported separately.There is controversy over the quality assessment of qualitative literature, with over 100 tools currently available, however, the reliability of these tools is questionable.[20] Some authors, claiming that setting standards, or following prescribed formulas, is a fruitless exercise, have questioned the entire process of quality appraisal.[19] Therefore, quality assessment of included papers was not undertaken.

Synthesis of the data, which involves some form of transformation, was not performed. There are many different methodologies for the synthesis of qualitative work with differing approaches, inconsistent and confusing nomenclature, and the prolific use of modification of techniques.[21] Furthermore, the synthesis of qualitative data is in itself a controversial topic, with some authors questioning if it should be attempted at all.[19] Issues surrounding the synthesis include those of mixing methods and researchers.[22] However, our aim here was not to synthesise or transform the studies, but to provide a map, or a picture of the whole. This is consistent with approaches described in the literature.[17-19,21,22] Our approach involved identifying themes that the authors had recognised as important to decision making. Themes and, where appropriate, sub-themes are reported as per the authors' classification. Therefore the authors' own findings, in their own words as far as possible, are reported, and any clear consistencies or inconsistencies are discussed. The lead author completed this process, and the findings were cross-checked by another experienced qualitative researcher (AR).

Results

The electronic database search returned 556 papers. In total, 70 papers remained after a title review, and a further 50 papers were excluded on the basis of their abstract. A further 11 papers were retrieved for full text review from the bibliographic search (total 31 papers full text review). Of these, seven were included in the review.

Table I. Basic study characteristics

Author	Title	Setting	Sampling	Participants	Method	Analysis
Figaro et al[23]	Preferences for Arthritis Care Amoung Urban African Americans: "I Don't Want to Be Cut".	Church or senior centre in Manhatton, New York.	Opt-in recruitment from patients who had pain or stiffness in one or both knees.	A total of 94 African American/black participants, (79 female, 15 male). Mean age 71 years. 82 without and 12 with knee arthroplasty.	Structured interviews	Content analysis using constant comparative method
Suarez-Almazor[24]	A qualitative Analysis of Decision-Making for Total Knee Replacement in patients with Osteoarthritis.	Primary care setting in United States.	Patients identified as subpopulation of another study, with a diagnosis of knee OA but no TKA.	A total of 37 patients. 13 white, nine Hispanic, 15 African American (14 males, 23 females). Mean age 64 years.	Focus group	Thematic analysis using a grounded theory approach.
Chang et al[25]	Concerns of Patients Actively Contemplating Total Knee Replacement: Differences by Race and Gender.	Othopaedic surgeon's office, United States.	Patients actively considering knee arthroplasty. Patients were recruited in sequence of attendance.	A total of 12 male, 25 female: 20 white American, 17 African American. Mean age 60 years.	Focus group	Thematic content analysis
Al-Taiar et al[26]	Attitudes to knee osteoarthritis and total knee replacement in Arab women: a qualitative study.	The only publicly funded orthopaedic centre in Kuwait.	Patients selected from the waiting list for knee replacement. Process not reported.	A total of 39 Kuwaiti female participants. Mean age 62.5 years.	Semi-structured focus group	Thematic analysis
Toye et al[27]	Personal meanings in the construction of need for total knee replacement surgery.	Specialist orthopaedic centre, England, UK.	Patient on waiting list for TKA and below average need as judged by WOMAC pain and function score. Invited by letter (opt in).	A total of 18 patients (12 male, six female). Mean age and ethnicity not reported.	Semi-structured interviews	Interpretive phenomenological analysis
Woolhead et al[28]	Who should have priority for a knee joint replacement?	Three orthopaedic surgeons' waiting lists, UK.	Patients on the waiting list for knee replacement. Sampling across age and gender by letter (opt in).	A total of 25 participants (14 female, 11 male). Mean age 65 years.	Semi-structured interviews	Constant comparison
Marcinkowski et al[29]	Getting Back to the Future. A Grounded Theory Study of the Patient Perspective of Total Knee Joint Arthoplasty.	A publicly funded centre in New Zealand.	Purposive sampling by age, gender, comorbidity and complications from patients who had recently had a knee arthroplasty.	A total of nine European New Zealand participants (four male, five female). Mean age 71 years.	Unstructured interview	Constant comparative analysis based in grounded theory

OA, osteoarthritis; TKA, total knee arthroplasty; WOMAC, Western Ontario and McMaster Universities Arthritis Index

A flow diagram of the included studies is displayed in Figure 1.

The basic study characteristics can be found in Table I.[23-29]

Study characteristics. The included studies have examined decision making in a population with knee symptoms but no diagnosis of knee pain,[23] patients in primary care with a diagnosis of knee OA,[24] patients actively considering knee arthroplasty in secondary care,[25] patients on the waiting list,[26-28] and recent post-operative patients.[29] Of note, two papers had a focus that was not decision making in knee arthroplasties, but reported factors that influenced patients in making a decision, thus, both papers were included.

From the seven studies, four different countries are represented with 234 participants. Study samples range from nine to 94 participants (mean 33 participants). Of the 234 participants, 126 are African American (skewed by one large study of 94 participants),[23] with 39 Kuwaiti women, 33 "white" or "white American", nine European New Zealanders, with two studies (43 participants) not reporting ethnicity. Three studies conducted focus groups, with four conducting interviews. Analysis was reported in a variety of ways, with different nomenclature. In total, 68 out of the 234 participants (29%) were male.

Study themes. A matrix of study themes has been produced, demonstrating where themes overlap, and where they do not. The description of themes is taken from the relevant papers, but summarised where necessary. No synthesis or second order interpretation took place. Some ten themes were identified in more than one study: expectations of surgery; coping mechanisms; relationship with clinician; fear; pain; function; psychological implications; social network; previous experience of surgery; and conflict in opinions.

Expectation of surgery was a theme identified in five of the seven studies. A common finding was the uncertainty surrounding the outcome of a knee arthroplasty.

Four studies identified various patterns of coping mechanisms, which were important in the decision making process. The use of alternative medicine and social support was prevalent. Two studies identified religion as part of the preferred coping mechanism. These mechanisms help people live with OA and therefore predominantly act as deterrents to operative intervention, however, they can also act as stimulators (e.g. social support in helping to make the decision).

The relationship with the clinician was recognised as important in four studies. This was almost universally seen as a major factor in decision making, however, one paper found that trust in physicians was not an important factor. Related to this theme, two papers documented the role of decisional conflict in decision making. Woolhead et al,[28] who examined patients' views on prioritisation for surgery, found that decisional conflict existed because of differences of opinion between patient and surgeon. This was consistent with findings from Suarez-Almazor et al.[24] Interestingly, patients in these studies interacted with primary care physicians and surgeons, suggesting conflict continues throughout the patients' journey to knee arthroplasty.

Many fears were identified in the studies. This was predominantly a fear of the operation (with associated anaesthesia), recovery, and outcome. One fear was related to pain, which was identified in four of the studies, with the effect on participants' life being a major factor in decision making.

Function was reported in three studies as a decision making factor. Many authors linked function with another domain (e.g. Marcinkowski et al[29] describe physical and emotional struggling as a theme).

Psychological aspects were explored in three papers. This was viewed quite consistently across papers involving participants on the waiting list, or those who had received knee arthroplasties. Feelings of frustration, vulnerability, letting others down, and self-image were discussed.

Patients' social network functioned both as a source of perceived pressure and as an information source related to the social network's experience of surgery. Related to this was a personal experience of surgery, identified by two studies.

Six further themes were identified in the studies, but were only identified in one sample of patients. These included surgery as a last resort, preference for continuing their current state, financial issues, different source of information, and different preferences for participation in decision making.

Discussion

We describe a heterogeneous group of studies examining the decision making process of patients when considering knee arthroplasty. Some themes are remarkably consistent, others have only been demonstrated in specific samples of patients. One theme, the relationship with the treating physician, was not found to be important in one study, contrasting with it being a major factor in four other papers. It may be that this is a result of the study samples: the study that found this theme was not important as it included patients that had been seen by many doctors in many different countries.

The themes identified within this review are consistent with the wider literature of knee arthroplasties. Huduk et al[30] investigated a population of patients with hip and knee OA who had elected not to have an arthroplasty. Patients who do not proceed to joint arthroplasty tend to view OA as an inevitable part of ageing, see others as worse off than themselves, and wait for the doctor to recommend it. These findings are consistent with findings from our review, especially with the samples of patients who were at an earlier stage in their treatment course. This aspect is key in understanding the high rate of patients who are unwilling to consider knee arthroplasty.[9]

Elwyn and Miron-Shatz[31] suggested that the decision making process can be split into deliberation and decision making. This would suggest that the deliberation process occurs until the decision to have surgery is reached (what Clark et al[32] refer to as the "Decision Making Threshold"). Included studies demonstrated that patients experience decisional conflict, however, it is unclear if this conflict causes a degree of stress during the deliberation stage, or if this is resolved once the threshold is reached. It is also unclear if patients would be willing to move back into the deliberation phase if their symptoms improved. The relationship between the decision making threshold and the movement from deliberation to decision making is currently poorly understood, and should be a focus for further research.

In 2007 O'Neill et al[11] conducted a qualitative meta-synthesis of decision making in joint arthroplasty. This study concluded that social and cultural categories shape patients' expectations of treatment options. Coping strategies and life context determined the short- and longer-term outcomes of joint arthroplasty. Interestingly, the strongest theme identified was trust in the health professional. This is broadly consistent with the findings of this review, however, one paper reports a notable exception.[26]

In 2012 Jayadev[7] conducted a review on patient decision aids. This included evidence from a Cochrane review that concluded that decision aids improved patient knowledge, resulted in less decisional conflict, less indecision, and greater concordance between patient values and chosen options. However, it also commented on the varying quality of decision aids, finding that the content regarding different treatment options was commonly lacking. Compounding this, our review would suggest that there are various concerns that patients have over and above the different treatment options (e.g. the "relationship with the clinician"). Using the findings from this review, there is the potential to tailor the information in decision aids to address patients' major concerns.

This review is prone to various weaknesses. The indexing of qualitative work from electronic databases is not as well developed as that of quantitative studies.[21] There are currently no registers of qualitative work and studies that commonly use descriptive or imaginative titles, making identification through standard search techniques problematic.[19,21] To address this, a broad based approach, searching for only the subject and topic terms was used.[19] This results in a large number of irrelevant studies, and, with an estimated 23% of studies not having indexed abstracts, results in a large number of full text articles being screened.[19] Furthermore, we conducted a comprehensive bibliographic search of all full text articles retrieved, including those excluded from the review. This approach is consistent with that used by the Evidence for Policy and Practice Information Centre.[19]

The definition of a qualitative study is problematic, with experienced qualitative researchers disagreeing over what constitutes qualitative.[19] We addressed this by having strict criteria – practically this was achieved by only including research that, in the authors' opinion, was unequivocally qualitative in nature. Studies examining knee arthroplasty decision making with other conditions (e.g. hip arthroplasty or back pain) were excluded.[11,33,34] These studies may have contained useful information, but were excluded on the basis that the themes may not have been relevant to knee arthroplasty decision making.

No synthesis of the data took place, although common themes have been highlighted. This is a controversial subject in itself, as is providing a narrative review of qualitative research.[18,19,21] Our aim was to provide an overview of what is known about how patients make decisions, and to let the reader interpret the themes expressed from each paper.

Various weaknesses were present in the studies included within this review. Some samples of patients were homogeneous within certain characteristics (e.g. black African Americans).[23] Additionally, the stage of the decision making process has not been addressed, with each included study focusing on one stage of the pathway of care. The stage of decision making is likely to be key to understanding the decision making process, and therefore these studies lack an essential dimension. We found it interesting that positive findings were reported throughout all studies and only one study mentioned a negative result.[26] It is unclear if authors did not report negative findings, or did not make any attempts to investigate certain factors that could affect decision making. This could be thought of as a reporting bias. To what degree this influenced the result is unclear.

An additional aspect, that has became relevant recently is that of providing a personalised prediction of outcome for patients considering knee arthroplasty and which has been identified as a research priority by the National Institute for Health and Clinical Excellence (NICE).[35] Currently there are several investigations into the development of such a tool.[36-39] It is unclear how such a tool would affect decision making.

The strengths of this study are the systematic method of identifying studies, the accurate reporting of themes from individual papers, and the process of cross-validating the themes that were extracted from the papers.

We identified 17 individual themes across seven studies that covered all stages of the decision making journey, from developing symptoms through to recovery after knee arthroplasty. Ten themes were repeated across studies, with fear, pain, coping mechanisms, expectations of surgery, and the relationship with the clinician seen most frequently.

Understanding all facets that may affect patient decision making when considering knee arthroplasty is essential to the shared decision making process. This work can act as a framework for understanding common concerns of patients considering knee arthroplasty and aid clinicians in delivering patient-centred care. Other methods of delivering information to patients (e.g. patient decision aids) should address these factors. However, how best to integrate these findings into information delivery systems for patients is an area that requires greater understanding.

By facilitating the patient–doctor interaction, a sound understanding of patient decision making has the potential to address increasing financial pressures, variation in uptake, and improved satisfaction from surgery and the decision making process itself.

Supplementary material

ë A table showing themes is available alongside the online version of this article at www.bjr.boneandjoint.org.uk

References

1. **No authors listed.** Clinical Surgical Practice Issues 2012. British Orthopaedic Association. http://www.boa.ac.uk/PP/Pages/clin-issues.aspx (date last accessed 16 July 2015).
2. **Gonzalez Saenz de Tejada M, Escobar A, Bilbao A, et al.** A prospective study of the association of patient expectations with changes in health-related quality of life outcomes, following total joint replacement. *BMC Musculoskelet Disord* 2014;15:248.
3. **No authors listed.** National Joint Registry 2015. http://www.njrcentre.org.uk/njrcentre/default.aspx (date last accessed 16 July 2015).
4. **No authors listed.** The Autumn Statement: NHS Funding. The King's Fund. http://www.kingsfund.org.uk/publications/articles/autumn-statement (date last accessed 16 July 2015).
5. **Culliford D, Maskell J, Judge A, et al.** Future projections of total hip and knee arthroplasty in the UK: results from the UK Clinical Practice Research Datalink. *Osteoarthritis Cartilage* 2015;23:594–600.
6. **Stacey D, Bennett CL, Barry MJ, et al.** Decision aids for people facing health treatment or screening decisions. *Cochrane Database Syst Rev* 2011;10:CD–001431.
7. **Jayadev C, Khan T, Coulter A, Beard DJ, Price AJ.** Patient decision aids in knee replacement surgery. *Knee* 2012;19:746–750.
8. **No authors listed.** Atlas of Variation 2010. RightCare. http://www.rightcare.nhs.uk/index.php/programme/ (date last accessed 16 July 2015).
9. **Hawker GA, Wright JG, Badley EM, Coyte PC.** Perceptions of, and willingness to consider, total joint arthroplasty in a population-based cohort of individuals with disabling hip and knee arthritis. *Arthritis Rheum* 2004;51:635–641.
10. **Berkhoff C.** Disparities in access and in quality of care in rheumatology. [abstract] *Ann Rheum Dis* 2013;71:10.
11. **O'Neill T, Jinks C, Ong BN.** Decision-making regarding total knee replacement surgery: a qualitative meta-synthesis. *BMC Health Serv Res* 2007;7:52.
12. **Bourne RB, Chesworth B, Davis A, Mahomed N, Charron K.** Comparing patient outcomes after THA and TKA: is there a difference? *Clin Orthop Relat Res* 2010;468:542–546.

13. **Bachmeier CJ, March LM, Cross MJ, et al.** A comparison of outcomes in osteoarthritis patients undergoing total hip and knee replacement surgery. *Osteoarthritis Cartilage* 2001;9:137–146.

14. **Ibrahim SA, Siminoff LA, Burant CJ, Kwoh CK.** Differences in expectations of outcome mediate African American/white patient differences in "willingness" to consider joint replacement. *Arthritis Rheum* 2002;46:2429–2435.

15. **Grotle M, Hagen KB, Natvig B, Dahl FA, Kvien TK.** Obesity and osteoarthritis in knee, hip and/or hand: an epidemiological study in the general population with 10 years follow-up. *BMC Musculoskelet Disord* 2008;9:132.

16. **Jokela M, Hintsanen M, Hakulinen C, et al.** Association of personality with the development and persistence of obesity: a meta-analysis based on individual-participant data. *Obes Rev* 2013;14:315–323.

17. **Sandelowski M, Barroso J, Voils CI.** Using qualitative metasummary to synthesize qualitative and quantitative descriptive findings. *Res Nurs Health* 2007;30:99–111.

18. **Pantoja T.** Sythesis methods in Systematic reviews of Health Policy and Systems Research. In: Note Af HB, ed. Alliance for HPSR Alliance for HPSR; 2011.http://www.who.int/alliance-hpsr/projects/alliancehpsr_briefingnotesynthesismethodschile.pdf (date last accessed 24 August 2015).

19. **No authors listed.** Centre for Reviews and Dissemination: Incorporating qualitative evidence in or alongside effectiveness reviews. https://www.york.ac.uk/media/crd/Systematic_Reviews.pdf (date last accessed 24 August 2015).

20. **Dixon-Woods M, Sutton A, Shaw R, et al.** Appraising qualitative research for inclusion in systematic reviews: a quantitative and qualitative comparison of three methods. *J Health Serv Res Policy* 2007;12:42–47.

21. **Barnett-Page E, Thomas J.** Methods for the synthesis of qualitative research: a critical review. *BMC Med Res Methodol* 2009;9:59.

22. **Walsh D, Downe S.** Meta-synthesis method for qualitative research: a literature review. *J Adv Nurs* 2005;50:204–211.

23. **Figaro MK, Russo PW, Allegrante JP.** Preferences for arthritis care among urban African Americans: "I don't want to be cut". *Health Psychol* 2004;23:324–329.

24. **Suarez-Almazor ME, Richardson M, Kroll TL, Sharf BF.** A qualitative analysis of decision-making for total knee replacement in patients with osteoarthritis. *J Clin Rheumatol* 2010;16:158–163.

25. **Chang HJ, Mehta PS, Rosenberg A, Scrimshaw SC.** Concerns of patients actively contemplating total knee replacement: differences by race and gender. *Arthritis Rheum* 2004;51:117–123.

26. **Al-Taiar A, Al-Sabah R, Elsalawy E, Shehab D, Al-Mahmoud S.** Attitudes to knee osteoarthritis and total knee replacement in Arab women: a qualitative study. *BMC Res Notes* 2013;6:406.

27. **Toye FM, Barlow J, Wright C, Lamb SE.** Personal meanings in the construction of need for total knee replacement surgery. *Soc Sci Med* 2006;63:43–53.

28. **Woolhead GM, Donovan JL, Chard JA, Dieppe PA.** Who should have priority for a knee joint replacement? *Rheumatology (Oxford)* 2002;41:390–394.

29. **Marcinkowski K, Wong VG, Dignam D.** Getting back to the future: a grounded theory study of the patient perspective of total knee joint arthroplasty. *Orthop Nurs* 2005;24:202–209.

30. **Hudak PL, Clark JP, Hawker GA, et al.** "You're perfect for the procedure! Why don't you want it?" Elderly arthritis patients' unwillingness to consider total joint arthroplasty surgery: a qualitative study. *Med Decis Making* 2002;22:272–278.

31. **Elwyn G, Miron-Shatz T.** Deliberation before determination: the definition and evaluation of good decision making. *Health Expect* 2010;13:139–147.

32. **Clark JP, Hudak PL, Hawker GA, et al.** The moving target: a qualitative study of elderly patients' decision-making regarding total joint replacement surgery. *J Bone Joint Surg [Am]* 2004;86-A:1366–1374.

33. **Dosanjh S, Matta JM, Bhandari M, Anterior THA Research Collaborative.** The final straw: a qualitative study to explore patient decisions to undergo total hip arthroplasty. *Arch Orthop Trauma Surg* 2009;129:719–727.

34. **Katz JN, Lyons N, Wolff LS, et al.** Medical decision-making among Hispanics and non-Hispanic Whites with chronic back and knee pain: a qualitative study. *BMC Musculoskelet Disord* 2011;12:78.

35. **No authors listed.** Osteoarthritis: Care and management in adults. National Institute for Health and Care Excellence. http://www.nice.org.uk/Guidance/CG177 (date last accessed 16 July 2015).

36. **Baker PN, Deehan DJ, Lees D, et al.** The effect of surgical factors on early patient-reported outcome measures (PROMS) following total knee replacement. *J Bone Joint Surg [Br]* 2012;94-B:1058–1066.

37. **Judge A, Arden NK, Cooper C, et al.** Predictors of outcomes of total knee replacement surgery. *Rheumatology (Oxford)* 2012;51:1804–1813.

38. **No authors listed.** Targeted rehabilitation to improve outcome after knee replacement (TRIO). Arthritis Research U.K. http://www.arthritisresearchuk.org/research/grant-tracker-items/2012/targeted-rehabilitation-to-improve-outcome-after-knee-replacement-trio.aspx (date last accessed 16 July 2015).

39. **Barlow T, Dunbar M, Sprowson A, Parsons N, Griffin D.** Development of an outcome prediction tool for patients considering a total knee replacement--the Knee Outcome Prediction Study (KOPS). *BMC Musculoskelet Disord* 2014;15:451.

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Author contributions:

- T. Barlow: Design, data collection, data analysis, writing the paper
- D. Griffin: Writing the paper
- D. Barlow: Data collection, data analysis, drafting paper
- A. Realpe: Design, data analysis, drafting paper

ICMJE Conflict of Interest:

- None declared

9.9 Appendix IX: Development of an outcome prediction tool for patients considering a total knee replacement - the Knee Outcome Prediction Study (KOPS).

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BMC Musculoskeletal Disorders

STUDY PROTOCOL **Open Access**

Development of an outcome prediction tool for patients considering a total knee replacement – the Knee Outcome Prediction Study (KOPS)

Tim Barlow, Mark Dunbar, Andrew Sprowson, Nick Parsons and Damian Griffin*

Abstract

Background: Knee osteoarthritis affects 10% of the UK population over 55 years, resulting in pain and decreased quality of life. Knee replacement surgery has a proven benefit, with over 85,000 performed each year in the UK; however, approximately 17% of people are dissatisfied after surgery. Consequently, some Primary Care Trusts have reduced the funding available for knee replacements.
Most previous work has focused on the effect of different prostheses and treatment protocols on patient's outcome. However, this has been unable to account for all the variability and there is growing evidence that patient factors may significantly affect outcome. How to identify these at risk patients has been identified as a research priority by the National Institute of Clinical Excellence, the British Orthopedic Association, and the National Joint Registry.
The aim of this study is to develop a clinically appropriate outcome prediction tool based on measurable predictors affecting outcome.

Methods/design: We propose a prospective cohort study, designed to develop and validate an outcome prediction tool based on patient factors.
Six hundred patients who are scheduled for total knee replacement secondary to primary osteoarthritis will be recruited before surgery from all six hospitals (NHS and private) that provide total knee replacements to the population of Coventry and Warwickshire (UK). Patients will complete a baseline assessment of patient factors before their operation and will be followed up at 6 and 12 months post surgery.

Discussion: A clinically appropriate outcome prediction tool will allow patients to make a more informed decision regarding surgery. Aligning patient expectations with a realistic prediction of outcome should improve satisfaction. Ultimately, this project is likely to inform national policy making and regional service provision.

Keywords: Total knee replacement, Patient factors, Outcome prediction tool

Background

Primary osteoarthritis (OA) of the knee is a condition that can lead to loss of knee function. This in turn can lead to difficulty working, performing activities of daily living, stress, and depression [1]. Ten percent of the U.K. population over the age of 55 suffers from pain as a result of knee OA [2]. With an ageing population, this condition will present an ever increasing health burden. Surgery in the form of total knee replacement has reliably been shown to have a beneficial effect [3], and 95,454 knee replacements were performed in England and Wales in 2013, with over 90% of these for OA [4]. However a sub group of patients exist who have poor outcomes following knee replacement. Some studies show chronic pain rates as high as 17% [5]. Most previous work has focused on the effect of different prostheses and treatment protocols on outcome. However these factors have proved insufficient to account for all the variability in the outcome, and there is growing evidence that patient factors may significantly affect outcome [6]. A patient factor can be defined as being any factor that is intrinsic to the patient and that is not rapidly changed by a change in environment. These factors may include demographic data, functional and

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general health scores as well as psychological attributes and radiographic appearances.

Several patient factors have been identified as accounting for some of the variance in outcome after knee replacement; however which patient factors are important, and how much they affect outcome remains uncertain.

Pre-operative functional scores have been shown in several studies to have a consistent correlation to post operative function scores [7-10]. This would suggest that patients who are operated on earlier in their clinical course have a better outcome.

Medical co-morbidity has also been shown to have an effect on postoperative function [5,9,11-13], although some studies of reasonable size have not found a correlation [6,7,10,14].

Psychosocial factors have been examined by several authors. Sharma [10] included the role function, emotional, social function and motivation subscales of the SF-36 in their hierarchical regression model, where an additional 19% of the variance of three-month post-op SF-36 PF was explained. Heck [7] and Lingard [9] used slightly different measures of mental health but both showed a significant association with postoperative physical function.

There is some evidence to suggest that an increased body mass index (BMI) is correlated with a worse absolute physical outcome. However, Spicer [14] noticed that there was no significant difference in the absolute improvement in physical outcome. Fortin [8] reported information on the change scores for preoperatively determined high function and low function groups. The lower function groups, although having lower absolute six month function scores, showed greater improvement than the high functioning group.

Age, gender and education had either non-significant results, or produced correlations that were too small to be of clinical significance in the above papers. However, it may be that these patient factors were, at least in part, confounded with one or other of the factors that showed positive associations with outcome.

Stratification of patient risk is currently the most important question in knee replacement surgery, and has been identified as a research priority by the U.K. National Institute of Health and Care Excellence [13].

Previous pilot work at out institution has identified measurable pre-operative patient factors that may affect outcome. The pilot work has allowed the development of a protocol that will enable measurement of the effect of different patient factors.

The primary aim of this study is to measure the effect of patient factors on outcome after knee replacementand to develop an outcome prediction tool for patients considering a total knee replacement. This tool could be used to empower patients to make a more informed decision about having a knee replacement, by allowing an accurate, personalised prediction of what they can expect.

Methods/design

We plan to undertake a prospective multi-centre cohort study including all six hospitals (NHS and private) that provide total knee replacements to the population of Coventry and Warwickshire. This represents a diverse population and basic demographic data will be compared to data from the National Joint Registry (NJR) [4] to allow comparison between the study population and the U.K. as a whole.

This study will use methodologies tested in a pilot study undertaken at our institution. This study tested the feasibility of the recruitment procedure and the type and presentation of questionnaires used to measure patient factors.

A consecutive series of patients presenting at clinics at each centre will be approached and if deemed eligible will be asked to consent to take part in the study. Our pilot study showed that this procedure is feasible and that 80% of eligible patients give consent to participate. Based on this figure, we expect to recruit about 60 patients per month, over a recruitment period from April 2013 to July 2014. This should provide a pool of over 1000 patients who are eligible for inclusion in the study, and over 800 who would consent to participate. We have set our recruitment target to be somewhat lower than this to allow for any unexpected recruitment problems. We do not anticipate any serious problems in reaching this target; however, the pilot study took place at one institution, and there may be a drop in recruitment rate when extending the study over multiple sites.

Patients will be recruited from their pre-operative clinic appointment where a baseline assessment of patient factors will take place. Factors assessed include: age; BMI; social support (measured by living alone); deprivation (postcode); knee status and knee pain (Oxford Knee Score - OKS); general health (Short Form-36 - SF-36, which has eight domains across two subscales (mental and physical functioning)); medical co-morbidity (Co-morbidity questionnaire); joint co-morbidity (Joint Co-morbidity questionnaire); psychological co-morbidity (Hospital Depression and Anxiety Score); helplessness and coping style (Arthritis Helplessness Index); expectation (Knee Expectation Questionnaire); and radiographic status (Ahlback Score).

Patients will then be followed up at six and twelve months by postal questionnaire using the OKS, the SF-36, and a satisfaction score.

Setting

Patients listed for a knee replacement within the entire Arden Primary Care Cluster (private and NHS hospitals) will be screened for eligibility.

The participating hospitals are: University Hospital Coventry (University Hospitals of Coventry and Warwickshire NHS Trust (UHCW)); Hospital of St. Cross, Rugby (UHCW); Warwick Hospital (South Warwickshire Hospital NHS Trust); George Elliot Hospital (George Eliot Hospital NHS Trust); BMI Meriden Hospital, Coventry; and Nuffield Hospital Warwick, Leamington Spa.

Eligibility criteria

Patient population inclusion criteria:

- Patients who have a diagnosis of primary osteoarthritis
- Managed with a primary total knee replacement during the study period
- Able to complete questionnaires and give informed consent
- Patients who are over 50 years

Patient population exclusion criteria:

- Those who are unable or unwilling to give informed consent
- Those whose knee replacement is a unicompartmental or a revision procedure

Outcome measures

The primary outcome measure is knee function as measured by the OKS [15] at one year after operation. This condition-specific measure is a 12-item Patient Reported Outcome Measure (PROM), specifically designed to test knee pain and function. It has been well validated for this group of patients and is used by the U.K. Department of Health in the National Joint Registry.

The secondary outcome measures are the SF-36 [16], a 36 item patient reported measure of general health, which measures eight domains of health, including both physical and mental wellbeing, and a satisfaction score (validated in the pilot work).

Additional data about the process of inpatient treatment will be collected to ensure that there are no important differences in the treatment experiences between patients (e.g. surgical technique or length of stay).

Sample size

We have designed this study to have an 80% power to detect associations, at the 5% level, between preoperative factors and outcome, with a correlation coefficient of 0.2. This will predict factors that account for more than 4% of the variation in the primary outcome measure, which is below the clinically detectable changes for the OKS. To do this we need to recruit 400 patients (calculation using the pwr package in R, which implements the methods of Cohen (1988) for a linear model) [17].

We plan to use cross-validation methods for model development. As this will effectively reduce the sample of data we use for model fitting by a small factor, we choose to increase the sample size by 20%. Therefore, we require 480 patients with complete follow-up data.

Similar cohort studies have demonstrated a loss to follow up of around 10-15% [5-10]. We expect a loss to follow-up of about 10-15%, but have allowed for 20%. Therefore, our cohort would have to recruit 600 participants to be able to ensure analysis of 480 patients.

Data analysis

The primary analysis will use multiple linear regression models to identify patient factors that are significantly associated with the OKS and the SF-36 (the primary and secondary outcome measures – both have been validated for this group of patients). Logistic regression models to assess dichotomous outcomes (satisfaction) will also be used. Other factors that may affect outcome (e.g. level of experience of surgeon) will also be incorporated into the model. Diagnostic analysis will be used to assess model assumptions. Cross-validation techniques (e.g. 10 fold cross validation) will be used to inform model building and predictive power [18].

In our study that validated the tools we are using, 2.4% of cases had missing data at baseline assessment. Patterns of missingness will be investigated, for instance using missingness as the response variable in a logistic regression model, to assess whether there is any non-random element to the missing data.

We expect a loss to follow up of 10-15% and will use complete case analysis of follow up data as the primary analysis. As a sensitivity analysis to explore the effects of missing data we will use multiple imputation using standardised methods available through statistical packages (e.g. Multiple Imputation using Chained Equations). Results of both imputational analysis and complete case analysis will be presented.

Factors that predict outcome will form part of a streamlined questionnaire. The statistical analysis will allow weighting of the included factors, providing an estimate of outcome. Therefore, the outcome prediction tool will consist of both a streamlined questionnaire, and an associated algorithm.

High-level analysis will be undertaken in R [19] and also some data management and validation in SPSS (IBM SPSS Statistics for Macintosh, Version 22.0.), under the direction of an experienced statistician (NP).

Regulatory approval

This study has been approved by the Northampton National Research Ethics Service (12/EM/0336), and all relevant local approvals at all participating sites.

Discussion

This paper describes the justification for conducting a multi-centre cohort study using patient factors to predict outcome in patients after knee replacement surgery. By measuring the patient factors that are associated with better or worse functional outcome, we plan to predict outcome in individual patients, and support clinical decision making, hence improving quality of care. It will also facilitate interpretation of evidence from published observational studies of different interventions by determining whether groups of patients were similar, and allow post-hoc adjustment of clinical effectiveness studies for risk profile. The ability to adjust samples for case mix is particularly topical in view of the recent National Joint Registry introduction of Patient Reported Outcome Measures for total knee replacement. This data is in line with Department of Health recommendations and is used in service allocation.

The main strength of this study is the breadth and comprehensiveness of the patient factors selected for inclusion in the model building process; many of these factors have previously been shown to correlate with important outcome after surgery. Another strength is the size and demographic of the patient population sampled, which includes both NHS and private patients.

Abbreviations

OA: Primary osteoarthritis; BMI: Body mass index; OKS: Oxford Knee Score; SF-36: General health Short Form questionnaire.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

TB participated in the design of the study, co-ordination and drafted the manuscript. TB, MD, AS, and DG conceived the project and TB is leading the trial. TB, MD, AS and DG procured the project funding and developed the protocol. TB co-ordinates the study, and recruits the participants. TB wrote the first and final draft of this manuscript. NP advised on the study methodology and the statistical analysis plan. All authors participated in the study design, provided feedback on drafts of this paper and read and approved the final manuscript.

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References

1. Smith BW, Zautra AJ: **The effects of anxiety and depression on weekly pain in women with arthritis.** *Pain* 2008, **138**(2):354–361.
2. Peat G, Thomas E, Duncan R, Wood L, Hay E, Croft P: **Clinical classification criteria for knee osteoarthritis :performance in the general population and primary care.** *Ann Rheum Dis* 2006, **65**(10):1363–1367.
3. Juni P, Reichenbach S, Dieppe P: **Osteoarthritis: Rational approach to treating the individual.** *Best Pract Res clin Rheumatol* 2006, **20**(4):721–740.
4. *National Joint Registry for England and Wales.* 2014. http://www.njrcentre.org.uk/njrcentre/Reports,PublicationsandMinutes/Annualreports/tabid/86/Default.aspx.
5. Hawker G, Wright J, Coyte P, Paul J, Dittus R, Croxford R, Katz B, Bombardier C, Heck D, Freund D: **Health-related quality of life after knee replacement.** *J Bone and Joint Surg Am* 1998, **80**(2):163.
6. Santaguida PL, Hawker GA, Hudak PL, Glazier R, Mahomed NN, Kreder HJ, Coyte PC, Wright JG: **Patient characteristics affecting the prognosis of total hip and knee joint arthroplasty: a systematic review.** *Can J Surg* 2008, **51**(6):428–436.
7. Heck DA, Robinson RL, Partridge CM, Lubitz RM, Freund DA: **Patient outcomes after knee replacement.** *Clin Orthop* 1998, **356**:95–110.
8. Fortin PR, Clarke AE, Joseph L, Liang MH, Tanzer M, Ferland D, Phillips C, Partridge AJ, Bélisle P, Fossel AH, Mahomed N, Sledge CB, Katz JN: **Outcomes of total hip and knee replacement: preoperative functional status predicts outcomes at six months after surgery.** *Arthritis Rheum* 1999, **42**(8):1723–1728.
9. Lingard EA, Katz JN, Wright EA, Sledge CB, Kinemax Outcomes Group: **Predicting the outcome of total knee arthroplasty.** *J Bone Joint Surg Am* 2004, **86-A**(10):2179–2186.
10. Sharma L, Sinacore J, Daugherty C, Kuesis DT, Stulberg SD, Lewis M, Baumann G, Chang RW: **Prognostic factors for functional outcome of total knee replacement: a prospective study.** *J Gerontol A Biol Schi Med Sci* 1996, **54**(4):M152–M157.
11. König A, Scheidler M, Rader C, Eulert J: **The need for a dual rating system in total knee arthroplasty.** *Clin Orthop Relat Res* 1997, **345**:161–167.
12. Wasielewski RC, Weed H, Prezioso C, Nicholson C, Puri RD: **Patient comorbidity relationship to outcomes of total knee arthroplasty.** *Clin Orthop* 1998, **356**:85–92.
13. National Institute for Health and Care Excellence: *Osteoarthritis: care and management in adults.* Available at http://www.nice.org.uk/guidance/cg177.
14. Spicer DD, Pomeroy DL, Badenhausen WE, Schaper LA Jr, Curry JI, Suthers KE, Smith MW: **Body mass index as a predictor of outcome in total knee replacement.** *Int Orthop* 2001, **25**(4):246–249.
15. Murray DW, Fitzpatrick R, Rogers K, Pandit H, Carr AJ, Dawson J: **The use of the Oxford hip and knee scores.** *J Bone Joint Surg Br* 2007, **89-B**(8):1010–1014.
16. Garratt AM, Ruta DA, Abdalla MI, Buckingham JK, Russell IT: **The SF36 health survey questionnaire: an outcome measure suitable for routine use within the NHS?** *BMJ* 1993, **306**:1440.
17. Cohen J: *Statistical power analysis for the behavioral sciences.* 2nd edition. Hillsdale, NJ: Lawrence Erlbaum; 1988.
18. Stone M: **Cross-validatory choice and assessment of statistical predictions.** *J R Stat Soc B* 1974, **36**:111–147.
19. R Core Team. R: *A language and environment for statistical computing.* Vienna, Austria: R Foundation for Statistical Computing; 2014. http://www.R-project.org/.

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References

1. Porcheret M, Healey E, Dziedzic K, Corp N, Howells N, Birrell F. Osteoarthritis: a modern approach to diagnosis and management. *Reports on the Rheumatic Diseases (Series 6)*. Arthritis Research UK, 2011. Available at: http://www.arthritisresearchuk.org/health-professionals-and-students/reports/hands-on/hands-on-autumn-2011.aspx
2. National Institute of Health and Care Excellence. Clinical Guidance 177. Osteoarthritis: Care and management in adults. http://www.nice.org.uk/guidance/cg177: NICE, 2014.
3. Arden N, Nevitt MC. Osteoarthritis: epidemiology. *Best Pract Res Clin Rheumatol 2006;20-1:3-25.*
4. Abbott T, Altman RD, Dimeff R, Fredericson M, Vad V, Vitanzo Jr P, Yadalam S, Levine R, Bisson B, Bhattacharyya S. Do hyaluronic acid injections delay total knee replacement surgery? *Arthritis and Rheumatism 2013;Conference:American College of Rheumatology/Association of Rheumatology Health Professionals Annual Scientific Meeting, ACR/ARHP 2013. Conference Publication: (var.pagings). 65 (pp S910-S911).*
5. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, Christy W, Cooke TD, Greenwald R, Hochberg M, et al. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. *Arthritis Rheum 1986;29-8:1039-49.*
6. Ahmed U, Anwar A, Savage RS, Costa ML, Mackay N, Filer A, Raza K, Watts RA, Winyard PG, Tarr J, Haigh RC, Thornalley PJ, Rabbani N. Biomarkers of early stage osteoarthritis, rheumatoid arthritis and musculoskeletal health. *Sci Rep 2015;5:9259.*
7. Dieppe PA, Lohmander LS. Pathogenesis and management of pain in osteoarthritis. *Lancet 2005;365-9463:965-73.*
8. Blagojevic M, Jinks C, Jeffery A, Jordan KP. Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis. *Osteoarthritis Cartilage 2010;18-1:24-33.*
9. Bastick AN, Belo JN, Runhaar J, Bierma-Zeinstra SM. What Are the Prognostic Factors for Radiographic Progression of Knee Osteoarthritis? A Meta-analysis. *Clin Orthop Relat Res 2015;473-9:2969-89.*
10. Leyland KM, Hart DJ, Javaid MK, Judge A, Kiran A, Soni A, Goulston LM, Cooper C, Spector TD, Arden NK. The natural history of radiographic knee osteoarthritis: a fourteen-year population-based cohort study. *Arthritis Rheum 2012;64-7:2243-51.*
11. Dieppe P, Cushnaghan J, Tucker M, Browning S, Shepstone L. The Bristol 'OA500 study': progression and impact of the disease after 8 years. *Osteoarthritis Cartilage 2000;8-2:63-8.*
12. National Institute for Health and Care Excellence. Osteoathritis: Care and management in adults. Available at: http://www.nice.org.uk/Guidance/CG177: NICE, 2014.
13. Brouwer RW, Huizinga MR, Duivenvoorden T, van Raaij TM, Verhagen AP, Bierma-Zeinstra SM, Verhaar JA. Osteotomy for treating knee osteoarthritis. *Cochrane Database Syst Rev 2014;12:Cd004019.*
14. Vasiliadis HS, Wasiak J. Autologous chondrocyte implantation for full thickness articular cartilage defects of the knee. *Cochrane Database Syst Rev 2010-10:Cd003323.*
15. Barlow T, Plant CE. Why we still perform arthroscopy in knee osteoarthritis: a multi-methods study. *BMC Musculoskelet Disord 2015;16-1:85.*

16. Mancuso CA, Ranawat CS, Esdaile JM, Johanson NA, Charlson ME. Indications for total hip and total knee arthroplasties. Results of orthopaedic surveys. *J Arthroplasty 1996;11-1:34-46.*
17. Registry NJ. National Joint Registry. Vol. 2015. Available at: http://www.njrcentre.org.uk/njrcentre/default.aspx.
18. Ranawat AS, Ranawat CS. The history of total knee arthroplasty. In: *The Knee Joint*: Springer Paris, 2012:699-707.
19. Culliford D, Maskell J, Judge A, Cooper C, Prieto-Alhambra D, Arden NK. Future projections of total hip and knee arthroplasty in the UK: results from the UK Clinical Practice Research Datalink. *Osteoarthritis Cartilage 2015;23-4:594-600.*
20. Juni P, Reichenbach S, Dieppe P. Osteoarthritis: rational approach to treating the individual. *Best Pract Res Clin Rheumatol. Vol. 20. 2006:721-40.*
21. Jenkins PJ, Clement ND, Hamilton DF, Gaston P, Patton JT, Howie CR. Predicting the cost-effectiveness of total hip and knee replacement: a health economic analysis. *Bone & Joint Journal 2013;95-B-1:115-21.*
22. Judge A, Arden NK, Cooper C, Kassim Javaid M, Carr AJ, Field RE, Dieppe PA. Predictors of outcomes of total knee replacement surgery. *Rheumatology (Oxford) 2012;51-10:1804-13.*
23. Dixon T, Shaw M, Ebrahim S, Dieppe P. Trends in hip and knee joint replacement: socioeconomic inequalities and projections of need. *Ann Rheum Dis 2004;63-7:825-30.*
24. Hawker GA, Badley EM, Croxford R, Coyte PC, Glazier RH, Guan J, Harvey BJ, Williams JI, Wright JG. A population-based nested case-control study of the costs of hip and knee replacement surgery. *Medical Care 2009;47-7:732-41.*
25. British Orthopaedic Association. Clinical Surgical Practice Issues. 2012. Available at: http://www.boa.ac.uk/PP/Pages/clin-issues.aspx:
26. Judge A, Arden Nk Fau, Kiran A, Price A F, Javaid Mk Fau, Beard D, Murray D, Field RE. Interpretation of patient-reported outcomes for hip and knee replacement surgery: identification of thresholds associated with satisfaction with surgery. *J Bone Joint Surg Br. 2012 Mar;94(3):412-8201.*
27. The King's Fund. The Autumn Statement: NHS Funding. 2014. Available at: http://www.kingsfund.org.uk/publications/articles/autumn-statement.
28. The Department of Health. Making the NHS more efficient and less bureaucratic. Policy document. 2013. Available at: http://www.gov.uk/government/policies/making-the-nhs-more-efficient-and-less-bureaucratic:
29. National Institute for Health and Care Excellence. Who we are. History of NICE. 2015. Available at: http://www.nice.org.uk/about/who-we-are:
30. Gooberman-Hill R, Sansom A, Sanders CM, Dieppe PA, Horwood J, Learmonth ID, Williams S, Donovan JL. Unstated factors in orthopaedic decision-making: a qualitative study. *BMC Musculoskelet Disord 2010;11:213.*
31. Right Care. Atlas of Variation 2010. Available at: http://www.rightcare.nhs.uk/index.php/programme/
32. Mota RE, Tarricone R, Ciani O, Bridges JF, Drummond M. Determinants of demand for total hip and knee arthroplasty: a systematic literature review. *BMC Health Serv Res 2012;12:225.*
33. Judge A, Welton NJ, Sandhu J, Ben-Shlomo Y. Equity in access to total joint replacement of the hip and knee in England: cross sectional study. *Bmj 2010;341:c4092.*
34. Hawker GA, Wright JG, Badley EM, Coyte PC. Perceptions of, and willingness to consider, total joint arthroplasty in a population-based cohort of individuals with disabling hip and knee arthritis. *Arthritis Rheum 2004;51-4:635-41.*
35. Ibrahim SA, Siminoff LA, Burant CJ, Kwoh CK. Differences in expectations of outcome mediate African American/white patient differences in "willingness" to consider joint replacement. *Arthritis Rheum 2002;46-9:2429-35.*

36. Hawker GA. Who, when, and why total joint replacement surgery? The patient's perspective. *Curr Opin Rheumatol 2006;18-5:526-30.*
37. Cross MJ, March LM, Lapsley HM, Tribe KL, Brnabic AJ, Courtenay BG, Brooks PM. Determinants of willingness to pay for hip and knee joint replacement surgery for osteoarthritis. *Rheumatology (Oxford) 2000;39-11:1242-8.*
38. Allen KD, Golightly YM, Callahan LF, Helmick CG, Ibrahim SA, Kwoh CK, Renner JB, Jordan JM. Race and sex differences in willingness to undergo total joint replacement: the Johnston County Osteoarthritis Project. *Arthritis Care Res (Hoboken) 2014;66-8:1193-202.*
39. Borkhoff C. Disparities in access and in quality of care in rheumatology. *Annals of the Rheumatic Disease 2013;Conference:Annual European Congress of Rheumatology of the European League Against Rheumatism, EULAR 2012 Berlin Germany. Conference Start: 20120606 Conference End: 9. Conference Publication: (var.pagings). 71.*
40. Nuttall D, Parkin D Fau - Devlin N, Devlin N. Inter-provider comparison of patient-reported outcomes: developing an adjustment to account for differences in patient case mix. *Health Econ 2015;24(1):41-54.*
41. Barlow T, Clarke T, Dunbar M, Metcalfe A, Griffin D. The effect of expectation on satisfaction in total knee replacements: a systematic review. *SpringerPlus 2016;5-167.*
42. Jayadev C, Khan T, Coulter A, Beard DJ, Price AJ. Patient decision aids in knee replacement surgery. *Knee 2012;19-6:746-50.*
43. Joosten EA, DeFuentes-Merillas L, de Weert GH, Sensky T, van der Staak CP, de Jong CA. Systematic review of the effects of shared decision-making on patient satisfaction, treatment adherence and health status. *Psychother Psychosom 2008;77-4:219-26.*
44. Dwamena F, Holmes-Rovner M, Gaulden CM, Jorgenson S, Sadigh G, Sikorskii A, Lewin S, Smith RC, Coffey J, Olomu A. Interventions for providers to promote a patient-centred approach in clinical consultations. *Cochrane Database Syst Rev 2012;12:Cd003267.*
45. Stacey D, Bennett CL, Barry MJ, Col NF, Eden KB, Holmes-Rovner M, Llewellyn-Thomas H, Lyddiatt A, Legare F, Thomson R. Decision aids for people facing health treatment or screening decisions. *Cochrane Database Syst Rev 2011-10:Cd001431.*
46. Right Care. Measuring Shared Decision Making. A review of the evidence. I2012. Available at: http://www.rightcare.nhs.uk:
47. Say R, Murtagh M, Thomson R. Patients' preference for involvement in medical decision making: a narrative review. *Patient Educ Couns 2006;60-2:102-14.*
48. Brom L, Hopmans W, Pasman HR, Timmermans DR, Widdershoven GA, Onwuteaka-Philipsen BD. Congruence between patients' preferred and perceived participation in medical decision-making: a review of the literature. *BMC Med Inform Decis Mak 2014;14:25.*
49. Garfield S, Smith F, Francis SA, Chalmers C. Can patients' preferences for involvement in decision-making regarding the use of medicines be predicted? *Patient Educ Couns 2007;66-3:361-7.*
50. National Institute for Health and Care Excellence. Quality Statement 6: Shared Decision Making. Available at: http://www.NICE.org.uk
51. General Medical Council. Good Medical Practice. 2013. Available at: http://www.gmc-uk.org.
52. Chassany O, Boureau F, Liard F, Bertin P, Serrie A, Ferran P, Keddad K, Jolivet-Landreau I, Marchand S. Effects of training on general practitioners' management of pain in osteoarthritis: a randomized multicenter study. *J Rheumatol 2006;33-9:1827-34.*
53. Patel S, Ngunjiri A, Hee SW, Yang Y, Brown S, Friede T, Griffiths F, Lord J, Sandhu H, Thistlethwaite J, Tysall C, Underwood M. Primum non nocere: shared informed decision making in low back pain--a pilot cluster randomised trial. *BMC Musculoskelet Disord 2014;15:282.*

54. ISRCTN Registry. Trial of Option Grid for Arthritis of the knee (TOGA): easy to use shared decision making tools for disadvantaged groups. ISRCTN Registry, 2015.
55. O'Neill T, Jinks C, Ong BN. Decision-making regarding total knee replacement surgery: a qualitative meta-synthesis. *BMC Health Serv Res 2007;7:52.*
56. Bourne RB, Chesworth B, Davis A, Mahomed N, Charron K. Comparing patient outcomes after THA and TKA: Is there a difference? *Clinical Orthopaedics and Related Research 2010;468-2:542-6.*
57. Bachmeier CJ, March LM, Cross MJ, Lapsley HM, Tribe KL, Courtenay BG, Brooks PM. A comparison of outcomes in osteoarthritis patients undergoing total hip and knee replacement surgery. *Osteoarthritis Cartilage 2001;9-2:137-46.*
58. Grotle M, Hagen KB, Natvig B, Dahl FA, Kvien TK. Obesity and osteoarthritis in knee, hip and/or hand: an epidemiological study in the general population with 10 years follow-up. *BMC Musculoskelet Disord 2008;9:132.*
59. Jokela M, Hintsanen M, Hakulinen C, Batty GD, Nabi H, Singh-Manoux A, Kivimaki M. Association of personality with the development and persistence of obesity: a meta-analysis based on individual-participant data. *Obes Rev 2013;14-4:315-23.*
60. Sandelowski M, Barroso J, Voils CI. Using Qualitative Metasummary to Synthesize Qualitative and Quantitative Descriptive Findings. *Res Nurs Health 2007;30-1:99-111.*
61. Pantoja T. Sythesis methods in Systematic reviews of Health Policy and Systems Research. Briefing note. Methodology Centre for Systematic Reviews of Health Policy & Systems Research in Low- and Middle-Income Countries. 2011. Available at: http://www.who.int/alliance-hpsr/projects/alliancehpsr_briefingnotesynthesismethodschile.pdf
62. Centre for Reviews and Dissemination. Incorporating qualitative evidence in or alongside effetiveness reviews. 2008. Available at: https://www.york.ac.uk/crd/SysRev/!SSL!/WebHelp/6_1_Introduction_To_Incorporating_Qualitative_Evidence_In_Or.htm
63. Dixon-Woods M, Sutton A, Shaw R, Miller T, Smith J, Young B, Bonas S, Booth A, Jones D. Appraising qualitative research for inclusion in systematic reviews: a quantitative and qualitative comparison of three methods. *J Health Serv Res Policy 2007;12-1:42-7.*
64. Barnett-Page E, Thomas J. Methods for the synthesis of qualitative research: a critical review. *BMC Med Res Methodol 2009;9:59.*
65. Walsh D, Downe S. Meta-synthesis method for qualitative research: a literature review. *J Adv Nurs 2005;50-2:204-11.*
66. PRISMA. Preferred Reporting Items for Systematic Reviews and Meta-Analyses. 2012. Available at: http://www.prisma-statement.org/index.htm.
67. Figaro MK, Russo PW, Allegrante JP. Preferences for arthritis care among urban African Americans: "I don't want to be cut". *Health Psychol 2004;23-3:324-9.*
68. Suarez-Almazor ME, Richardson M, Kroll TL, Sharf BF. A qualitative analysis of decision-making for total knee replacement in patients with osteoarthritis. *J Clin Rheumatol 2010;16-4:158-63.*
69. Chang HJ, Mehta PS, Rosenberg A, Scrimshaw SC. Concerns of patients actively contemplating total knee replacement: differences by race and gender. *Arthritis Rheum 2004;51-1:117-23.*
70. Al-Taiar A, Al-Sabah R, Elsalawy E, Shehab D, Al-Mahmoud S. Attitudes to knee osteoarthritis and total knee replacement in Arab women: a qualitative study. *BMC Res Notes 2013;6:406.*
71. Toye FM, Barlow J, Wright C, Lamb SE. Personal meanings in the construction of need for total knee replacement surgery. *Soc Sci Med 2006;63-1:43-53.*
72. Woolhead GM, Donovan JL, Chard JA, Dieppe PA. Who should have priority for a knee joint replacement? *Rheumatology (Oxford) 2002;41-4:390-4.*

73. Marcinkowski K, Wong VG, Dignam D. Getting back to the future: a grounded theory study of the patient perspective of total knee joint arthroplasty. *Orthop Nurs 2005;24-3:202-9.*
74. Hudak PL, Clark JP, Hawker GA, Coyte PC, Mahomed NN, Kreder HJ, Wright JG. "You're perfect for the procedure! Why don't you want it?" Elderly arthritis patients' unwillingness to consider total joint arthroplasty surgery: a qualitative study. *Med Decis Making 2002;22-3:272-8.*
75. Elwyn G, Miron-Shatz T. Deliberation before determination: the definition and evaluation of good decision making. *Health Expect 2010;13-2:139-47.*
76. Clark JP, Hudak PL, Hawker GA, Coyte PC, Mahomed NN, Kreder HJ, Wright JG. The moving target: a qualitative study of elderly patients' decision-making regarding total joint replacement surgery. *J Bone Joint Surg Am 2004;86-a-7:1366-74.*
77. Dosanjh S, Matta JM, Bhandari M. The final straw: a qualitative study to explore patient decisions to undergo total hip arthroplasty. *Arch Orthop Trauma Surg 2009;129-6:719-27.*
78. Katz JN, Lyons N, Wolff LS, Silverman J, Emrani P, Holt HL, Corbett KL, Escalante A, Losina E. Medical decision-making among Hispanics and non-Hispanic Whites with chronic back and knee pain: a qualitative study. *BMC Musculoskelet Disord 2011;12:78.*
79. Miles M, Huberman M. Qualitative Data Analyis: An expanded Sourcebook. *Vol. 2, 2 ed. London: SAGE Publication, 1994:337.*
80. Coventry City Council. Local information and statistics. 2016. Available at: http://www.coventry.gov.uk/info/9/local_information_and_statistics
81. Office for National Statistics. Census data. 2016. Available at: https://www.ons.gov.uk/census
82. Barlow T, Dunbar M, Sprowson A, Parsons N, Griffin D. Development of an outcome prediction tool for patients considering a total knee replacement--the Knee Outcome Prediction Study (KOPS). *BMC Musculoskelet Disord 2014;15-1:451.*
83. Braun V, Clarke V. Using thematic analysis in psychology. *Qualitative Research in Psychology 2006;3-2:77-101.*
84. QSR International Pty Ltd. NVivo qualitative data analysis software. 10 ed, 2012.
85. Freelon D. ReCal OIR: Ordinal, Interval, and Ratio Intercoder Reliability as a Web Service. *International Journal Of Internet Science 2013;8-1:10-6.*
86. Shenton A. Strategies for ensuring trustworthiness in qualitative research projects. *Education for Information 2004;22-22:63-75.*
87. Watkins E, Brown RG. Rumination and executive function in depression: an experimental study. *J Neurol Neurosurg Psychiatry 2002;72-3:400-2.*
88. Gonzalez Saenz de Tejada M, Escobar A, Bilbao A, Herrera-Espineira C, Garcia-Perez L, Aizpuru F, Sarasqueta C. A prospective study of the association of patient expectations with changes in health-related quality of life outcomes, following total joint replacement. *BMC Musculoskelet Disord 2014;15:248.*
89. Santaguida PL, Hawker GA, Hudak PL, Glazier R, Mahomed NN, Kreder HJ, Coyte PC, Wright JG. Patient characteristics affecting the prognosis of total hip and knee joint arthroplasty: a systematic review. *Canadian Journal of Surgery 2008;51-6:428-36.*
90. Heck DA, Robinson RL, Partridge CM, Lubitz RM, Freund DA. Patient outcomes after knee replacement. *Clin Orthop Relat Res 1998-356:93-110.*
91. Fortin PR, Clarke AE, Joseph L, Liang MH, Tanzer M, Ferland D, Phillips C, Partridge AJ, Belisle P, Fossel AH, Mahomed N, Sledge CB, Katz JN. Outcomes of total hip and knee replacement: preoperative functional status predicts outcomes at six months after surgery. *Arthritis Rheum 1999;42-8:1722-8.*
92. Lingard EA, Katz JN, Wright EA, Sledge CB. Predicting the outcome of total knee arthroplasty. *J Bone Joint Surg Am. Vol. 86-A. United States, 2004:2179-86.*

93. Bourne RB, McCalden RW, MacDonald SJ, Mokete L, Guerin J. Influence of patient factors on TKA outcomes at 5 to 11 years followup. *Clin Orthop Relat Res 2007;464:27-31.*
94. Franklin PD, Li W, Ayers DC. The Chitranjan Ranawat Award: functional outcome after total knee replacement varies with patient attributes. *Clinical Orthopaedics & Related Research 2008;466-11:2597-604.*
95. Baker PN, Deehan DJ, Lees D, Jameson S, Avery PJ, Gregg PJ, Reed MR. The effect of surgical factors on early patient-reported outcome measures (PROMS) following total knee replacement. *J Bone Joint Surg Br 2012;94-8:1058-66.*
96. das Nair R, Anderson P, Clarke S, Leighton P, Lincoln NB, Mhizha-Murira JR, Scammell BE, Walsh DA. Home-administered pre-surgical psychological intervention for knee osteoarthritis (HAPPiKNEES): study protocol for a randomised controlled trial. *Trials 2016;17-1:54.*
97. Sharot T. The optimism bias. *Curr Biol 2011;21-23:R941-5.*
98. Dunbar M. Patient factors associated with outcome after total knee replacement: research towards the design of a multicenter prospective cohort study. *Warwick Medical School. PhD. 2008*.
99. Van Beeck A, Clockaerts S, Somville J, Van Heeswijk JH, Van Glabbeek F, Bos PK, Reijman M. Does infrapatellar fat pad resection in total knee arthroplasty impair clinical outcome? A systematic review. *Knee 2013;20-4:226-31.*
100. van der Voort P, Pijls BG, Nouta KA, Valstar ER, Jacobs WC, Nelissen RG. A systematic review and meta-regression of mobile-bearing versus fixed-bearing total knee replacement in 41 studies. *Bone & Joint Journal 2013;95-B-9:1209-16.*
101. Hetaimish BM, Khan Mm, Simunovic N, Al-Harbi Hh, Bhandari, Zalzal PK. Meta-analysis of navigation vs conventional total knee arthroplasty. *J Arthroplasty. 2012;27(6):1177-82.*
102. Hadi M, Barlow T, Ahmed I, Dunbar M, McCulloch P, Griffin D. Does malalignment affect revision rate in total knee replacements: a systematic review of the literature. *Springerplus 2015;4:835.*
103. Dunbar M, Barlow T, Griffin D. A systematic review of the association of patient factors with outcome after total knee replacement. 2012. Available at: http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42012002197.
104. Egger M, Schneider M, Davey Smith G. Spurious precision? Meta-analysis of observational studies. *BMJ 1998;316-7125:140-4.*
105. Geneletti S, Best N, Toledano MB, Elliott P, Richardson S. Uncovering selection bias in case-control studies using Bayesian post-stratification. *Stat Med 2013;32-15:2555-70.*
106. Razmjou H, Yee A, Ford M, Finkelstein JA. Response shift in outcome assessment in patients undergoing total knee arthroplasty. *Journal of Bone and Joint Surgery Series A 2590;88-12:2590-5.*
107. Fitzpatrick R, Davey C, Buxton MJ, Jones DR. Evaluating patient-based outcome measures for use in clinical trials. *Health Technol Assess 1998;2-14:i-iv, 1-74.*
108. Insall JN, Dorr LD, Scott RD, Scott WN. Rationale of the Knee Society clinical rating system. *Clin Orthop Relat Res 1989-248:13-4.*
109. Lingard EA, Katz JN, Wright RJ, Wright EA, Sledge CB. Validity and responsiveness of the Knee Society Clinical Rating System in comparison with the SF-36 and WOMAC. *J Bone Joint Surg Am 2001;83-A-12:1856-64.*
110. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol 2010;25-9:603-5.*
111. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in

meta-analyses. 2014. Available at:
http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
112. Murray DW, Fitzpatrick R, Rogers K, Pandit H, Beard DJ, Carr AJ, Dawson J. The use of the Oxford hip and knee scores. *J Bone Joint Surg Br 2007;89-8:1010-4.*
113. Collins NJ, Misra D, Felson DT, Crossley KM, Roos EM. Measures of Knee Function. *Arthritis care & research 2011;63-0 11:S208-S28.*
114. Garratt AM, Ruta DA, Abdalla MI, Buckingham JK, Russell IT. The SF36 health survey questionnaire: an outcome measure suitable for routine use within the NHS? *BMJ : British Medical Journal 1993;306-6890:1440-4.*
115. Jones CA, Voaklander DC, Suarez-Alma ME. Determinants of function after total knee arthroplasty. *Phys Ther 2003;83-8:696-706.*
116. Lim JT, Luscombe KL, Jones PW, White SH. The effect of preoperative symptom severity on functional outcome of total knee replacement--patients with the lowest preoperative scores achieve the lowest marks. *Knee.* Vol. 13. England, 2006:216-9.
117. Nunez M, Nunez E, del Val JL, Ortega R, Segur JM, Hernandez MV, Lozano L, Sastre S, Macule F. Health-related quality of life in patients with osteoarthritis after total knee replacement: factors influencing outcomes at 36 months of follow-up. In: *Osteoarthritis Cartilage.* Vol. 15. England, 2007:1001-7.
118. Cushnaghan J, Bennett J, Reading I, Croft P, Byng P, Cox K, Dieppe P, Coggon D, Cooper C. Long-term outcome following total knee arthroplasty: a controlled longitudinal study. *Annals of the Rheumatic Diseases 2009;68-5:642-7.*
119. Rajgopal V, Bourne RB, Chesworth BM, MacDonald SJ, McCalden RW, Rorabeck CH. The impact of morbid obesity on patient outcomes after total knee arthroplasty. *Journal of Arthroplasty 2008;23-6:795-800.*
120. Lopez-Olivo MA, Landon GC, Siff SJ, Edelstein D, Pak C, Kallen MA, Stanley M, Zhang H, Robinson KC, Suarez-Almazor ME. Psychosocial determinants of outcomes in knee replacement. *Annals of the Rheumatic Diseases 2011;70-10:1775-81.*
121. Nunez M, Lozano L, Nunez E, Segur J-M, Sastre S. Factors influencing health-related quality of life after TKA in patients who are obese. *Clinical Orthopaedics & Related Research 2011;469-4:1148-53.*
122. Sharma L, Sinacore J, Daugherty C, Kuesis DT, Stulberg SD, Lewis M, Baumann G, Chang RW. Prognostic factors for functional outcome of total knee replacement: a prospective study. *J Gerontol A Biol Sci Med Sci 1996;51-4:M152-7.*
123. Núñez M, Lozano L, Núñez E, Segur JM, Sastre S, Maculé F, Ortega R, Suso S. Total knee replacement and health-related quality of life: Factors influencing long-term outcomes. *Arthritis & Rheumatism: Arthritis Care & Research 2009;61-8:1062-9.*
124. Gandhi R, Razak F, Davey JR, Mahomed NN. Metabolic syndrome and the functional outcomes of hip and knee arthroplasty. *Journal of Rheumatology 2010;37-9:1917-22.*
125. Dowsey MM, Liew D, Stoney JD, Choong PF. The impact of pre-operative obesity on weight change and outcome in total knee replacement: a prospective study of 529 consecutive patients. *Journal of Bone & Joint Surgery, British Volume 2010;92-4:513-20.*
126. Kiebzak GM, Campbell M, Mauerhan DR. The SF-36 general health status survey documents the burden of osteoarthritis and the benefits of total joint arthroplasty: but why should we use it? *Am J Manag Care. Vol. 8. United States, 2002:463-74.*
127. Clement ND, MacDonald D, Howie CR, Biant LC. The outcome of primary total hip and knee arthroplasty in patients aged 80 years or more. *Journal of Bone & Joint Surgery Br 2011;93-9:1265-70.*
128. Sullivan M, Tanzer M, Stanish W, Fallaha M, Keefe FJ, Simmonds M, Dunbar M. Psychological determinants of problematic outcomes following Total Knee Arthroplasty. *Pain 2009;143-1-2:123-9.*
129. Lingard EA, Riddle DL. Impact of psychological distress on pain and function following knee arthroplasty. *J Bone Joint Surg Am 2007;89-6:1161-9.*

130. Pynsent PB, Adams DJ, Disney SP. The Oxford hip and knee outcome questionnaires for arthroplasty. *J Bone Joint Surg Br 2005;87-2:241-8.*
131. Stern JM, Simes RJ. Publication bias: evidence of delayed publication in a cohort study of clinical research projects. *Bmj 1997;315-7109:640-5.*
132. Haanstra TM, Van Den Berg T, Ostelo RW, Poolman RW, Jansma IP, Cuijpers P, de Vet HCW. Systematic review: Do patient expectations influence treatment outcomes in total knee and total hip arthroplasty? *Health and Quality of Life Outcomes 2012;10-152.*
133. Dyck BA, Zywiel MG, Mahomed A, Gandhi R, Perruccio AV, Mahomed NN. Associations between patient expectations of joint arthroplasty surgery and pre- and post-operative clinical status. *Expert Review of Medical Devices 2014;11-4:403-15.*
134. Waljee J, McGlinn EP, Sears ED, Chung KC. Patient expectations and patient-reported outcomes in surgery: A systematic review. *Surgery 2014;155-5:799-808.*
135. Steyer R, Schmitt M, Eid M. Latent State-Trait Theory and Research in Personality and Individual Differences. *European Journal of Personality 1999;13-13:389-408.*
136. Scott CE, Bugler KE, Clement ND, MacDonald D, Howie CR, Biant LC. Patient expectations of arthroplasty of the hip and knee. *J Bone Joint Surg Br 2012;94-7:974-81.*
137. Razmjou H, Yee A, Ford M, Finkelstein JA. Response Shift in Outcome Assessment in Patients Undergoing Total Knee Arthroplasty. *The Journal of Bone & Joint Surgery 2006;88-12:2590-5.*
138. Clement ND, Macdonald D, Patton JT, Burnett R. Post-operative Oxford knee score can be used to indicate whether patient expectations have been achieved after primary total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc. 2015 Jun;23(6):1578-90.*
139. Kumar M, Battepathi P, Bangalore P. Expectation fulfilment and satisfaction in total knee arthroplasty patients using the 'PROFEX' questionnaire. *Orthop Traumatol Surg Res. 2015;101(3):325-30.*
140. Adie S, Dao A, Harris IA, Naylor JM, Mittal R. Satisfaction with joint replacement in public versus private hospitals: a cohort study. *ANZ Journal of Surgery 2012;82-9:616-24.*
141. Vissers MM, Bussmann Jb, Verhaar Ja F, Busschbach Jj, Bierma-Zeinstra Sm, Reijman M. Psychological factors affecting the outcome of total hip and knee arthroplasty: a systematic review. *Semin Arthritis Rheum. 2012;41(4):576-88*
142. Lewis GN, Rice DA, McNair PJ, Kluger M. Predictors of persistent pain after total knee arthroplasty: a systematic review and meta-analysis. *Br J Anaesth. 2015;114(4):551-61*
143. Clement ND, MacDonald D, Burnett R. Primary total knee replacement in patients with mental disability improves their mental health and knee function: a prospective study. *Bone & Joint Journal 2013;95-B-3:360-6.*
144. Baert IA, Lluch E, Mulder T, Nijs J, Noten S, Meeus M. Does pre-surgical central modulation of pain influence outcome after total knee replacement? A systematic review. Osteoarthritis Cartilage. 2016 Feb;24(2):213-23..
145. Clement ND, MacDonald D, Simpson AH, Burnett R. Total knee replacement in patients with concomitant back pain results in a worse functional outcome and a lower rate of satisfaction. *Bone & Joint Journal 2013;95-B-12:1632-9.*
146. Clement ND, Jenkins PJ, MacDonald D, Nie YX, Patton JT, Breusch SJ, Howie CR, Biant LC. Socioeconomic status affects the Oxford knee score and short-form 12 score following total knee replacement. *Bone & Joint Journal 2013;95-B-1:52-8.*
147. Baker PN, Rushton S, Jameson SS, Reed M, Gregg P, Deehan DJ. Patient satisfaction with total knee replacement cannot be predicted from pre-operative variables alone: A cohort study from the National Joint Registry for England and Wales. *Bone & Joint Journal 2013;95-B-10:1359-65.*

148. Kiran A, Hunter DJ, Judge A, Field RE, Javaid MK, Cooper C, Arden NK. A novel methodological approach for measuring symptomatic change following total joint arthroplasty. *J Arthroplasty. 2014 Nov;29(11):2140-5.*
149. Riis A, Rathleff MS, Jensen MB, Simonsen O. Low grading of the severity of knee osteoarthritis pre-operatively is associated with a lower functional level after total knee replacement: a prospective cohort study with 12 months' follow-up. *Bone Joint J. 2014 Nov;96-B(11):1498-502.*
150. Konopka JF, Hansen VJ, Rubash HE, Freiberg AA. Risk assessment tools used to predict outcomes of total hip and total knee arthroplasty. *Orthop Clin North Am. 2015 Jul;46(3):351-62.*
151. Oxford University. ACHE and CORKA trials. 2016. Available at: http://www.ndorms.ox.ac.uk/clinical-trials
152. Arden N. Clinical Outcomes in Arthroplasty Study (COASt). Cinical Research Network Study Portfolio, 2016. Available at: https://www.crn.nihr.ac.uk/can-help/funders-academics/nihrcrn-portfolio/
153. Arthritis Research U.K.. Targeted rehabilitation to improve outcome after knee replacement (TRIO). 2015. Available at: http://www.arthritisresearchuk.org/research/grant-tracker-items/2012/targeted-rehabilitation-to-improve-outcome-after-knee-replacement-trio.aspx.
154. Brady TJ. Measures of self-efficacy. *Arthritis Care Res. 2011 Nov;63 Suppl 11:S473-85.*
155. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand 1983;67-6:361-70*
156. Dieppe PA, Reichenbach S Fau - Williams S, Williams S Fau - Gregg P, Gregg P Fau - Watt I, Watt I Fau - Juni P, Juni P. Assessing bone loss on radiographs of the knee in osteoarthritis: a cross-sectional study. *Arthritis Rheum. 2005 Nov;52(11):3536-41.*
157. Mahomed N, Gandhi R, Daltroy L, Katz JN. The Self-Administered Patient Satisfaction Scale for Primary Hip and Knee Arthroplasty. *Arthritis 2011;2011:591253.*
158. Montgomery LL, Tran KN, Heelan MC, Van Zee KJ, Massie MJ, Payne DK, Borgen PI. Issues of regret in women with contralateral prophylactic mastectomies. *Ann Surg Oncol 1999;6-6:546-52.*
159. Hillis SD, Marchbanks PA, Tylor LR, Peterson HB. Poststerilization regret: findings from the United States Collaborative Review of Sterilization. *Obstet Gynecol 1999;93-6:889-95.*
160. Beard DJ, Harris K, Dawson J, Doll H, Murray DW, Carr AJ, Price AJ. Meaningful changes for the Oxford hip and knee scores after joint replacement surgery. *Journal of Clinical Epidemiology 2015;68-1:73-9.*
161. R Core Team. A language and environment for statistical computing. *R Foundation for Statistical Computing.* Vienna, Austria, 2013.
162. Cohen J. *Statistical power analysis for the behavioral sciences.* 2nd ed., 1988.
163. Hawker G, Wright J, Coyte P, Paul J, Dittus R, Croxford R, Katz B, Bombardier C, Heck D, Freund D. Health-related quality of life after knee replacement. *J Bone Joint Surg Am 1998;80-2:163-73.*
164. IBM Corp. IBM SPSS Statistics for Macintosh, Version 22.0. *Armonk, NY: 2013.*
165. Field A. Discovering statistics using IBM SPSS statistics*. 4th ed.: SAGE, 2014.*
166. CAPITA. The quality of clinical coding in the NHS. Payment by results data assurance framework. Department of Health, 2014. Available at: http://www.gov.uk
167. Collins GS, Altman DG. An independent external validation and evaluation of QRISK cardiovascular risk prediction: a prospective open cohort study. *Bmj 2009;339:b2584.*
168. Judge A, Arden NK, Price A, Glyn-Jones S, Beard D, Carr AJ, Dawson J, Fitzpatrick R, Field RE. Assessing patients for joint replacement: can pre-operative

Oxford hip and knee scores be used to predict patient satisfaction following joint replacement surgery and to guide patient selection? *J Bone Joint Surg Br 2011;93-12:1660-4.*
169. Monitor. Best Practice Tariff. Department of Health, 2015. Available at: https://www.gov.uk/government/organisations/monitor
170. Ibrahim MS, Khan MA, Nizam I, Haddad FS. Peri-operative interventions producing better functional outcomes and enhanced recovery following total hip and knee arthroplasty: an evidence-based review. *BMC Med 2013;11:37.*
171. Rosenberger PH, Ickovics JR, Epel E, Nadler E, Jokl P, Fulkerson JP, Tillie JM, Dhabhar FS. Surgical stress-induced immune cell redistribution profiles predict short-term and long-term postsurgical recovery. A prospective study. *J Bone Joint Surg Am 2009;91-12:2783-94.*
172. Gaudilliere B, Fragiadakis GK, Bruggner RV, Nicolau M, Finck R, Tingle M, Silva J, Ganio EA, Yeh CG, Maloney WJ, Huddleston JI, Goodman SB, Davis MM, Bendall SC, Fantl WJ, Angst MS, Nolan GP. Coordinated Surgical Immune Signatures Contain Correlates of Clinical Recovery. *Science translational medicine 2014;6-255:255ra131-255ra131.*
173. Fragiadakis GK, Gaudilliere B, Ganio EA, Aghaeepour N, Tingle M, Nolan GP, Angst MS. Patient-specific Immune States before Surgery Are Strong Correlates of Surgical Recovery. *Anesthesiology 2015;123-6:1241-55.*